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TRANSACTIONS & STUDIES

of the

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Volume 16
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Number 1
(April 1948)

The Evaluation of BCG Vaccine in the Control of Tuberculosis*

By JOSEPH D. ARONSON, M.D.

THE honor of being selected as the recipient of the Alvarenga Prize is a great one. It is a distinction which I feel must be shared with my associates of the Indian Service whose splendid cooperation, for many years and at times under trying circumstances, made possible the carrying out of this study. To Dr. James Townsend, formerly Director of Health, Office of Indian Affairs, we are indebted for the interest and initiative in making this study possible. It has been a source of great gratification and satisfaction to have had the splendid cooperation of the more than 3000 Indian boys and girls and their families, and the interest that many of them have displayed in the course of this investigation.

In this day when there is so much interest in chemotherapeutic and antibiotic agents for treating and controlling tuberculosis, it is possible that there may be less concern about the use of specific immunizing agents as a method of curbing this disease.

The discovery of the tubercle bacillus in 1882 by Koch (1) gave impetus to numerous attempts to eradicate tuberculosis. The claims of Koch (2) in 1884, that a glycerol extract of the tubercle bacillus, or tuberculin, possessed protective and curative properties, was soon disproved. Since then numerous attempts have been made to induce specific resistance to tuberculosis by the use of fractions of the tubercle bacillus, its metabolic products, related acid-fast bacteria, heterologous strains of tubercle bacilli, or by the use of tubercle bacilli modified by chemical or physical procedures. Up to the present time none of these agents has succeeded in establishing definite resistance to infection by the tubercle bacillus.

The evolution and extent of tuberculosis depends not only upon the dosage and virulence of the infecting organism but also upon the frequency and interval between exposures, as well as upon undetermined constitutional factors.

There are many observed data, both clinical and experimental, which indicate that acquired resistance to tuberculous reinfection develops as a result of a previous tuberculous infection. This resistance, evidenced by the tendency to localization and limitation of the spread

* Alvarenga Prize Lecture VII (Award XLII), The College of Physicians of Philadelphia, 5 November 1947.

From the Health Division, Office of Indian Affairs, Department of the Interior, Washington, D. C., the Henry Phipps Institute, University of Pennsylvania, Philadelphia, and the Tuberculosis Control Division, U. S. Public Health Service.

and multiplication of the infecting organism, as well as by characteristic pathological changes, may not be as solid and as marked as the resistance resulting from infections with other bacteria, but it is definite.

Present day knowledge indicates that avirulent strains of tubercle bacilli are comparable with virulent strains in their chemical constitution, metabolism, ability to produce anatomical tubercles and to induce allergy. The essential difference is that the avirulent strains tend to localize, while the virulent strains generalize and produce progressive disease. It has been found, under experimental conditions, that in animals the highest degree of resistance follows infection with minute amounts of viable virulent tubercle bacilli or with larger amounts of viable attenuated strains of the organism. In this connection it is of great interest to call attention to the fact that the possibility of using attenuated viable tubercle bacilli for the purpose of protection against tuberculosis was suggested as long ago as 1889 by Dr. Samuel Dixon (3) of Philadelphia. He noted that guinea pigs, rabbits and opossums treated with old cultures containing pleomorphic and degenerated forms of tubercle bacilli showed resistance to reinfection with virulent tubercle bacilli. In 1894 De Schweinitz (4) of the Bureau of Animal Industry noted that a strain of tubercle bacillus grown on glycerol broth gradually lost its virulence and that, after 20 successive transplants on this medium, was no longer virulent for guinea pigs. This attenuated culture protected guinea pigs against reinfection with virulent tubercle bacilli.

In France, Calmette and Guerin (5) concluded from their extensive investigations dealing with the mechanism of tuberculous infection and immunity in cattle, that animals which had received a single small dose of finely divided virulent viable tubercle bacilli survived the initial infection, reacted to tuberculin and survived subsequent intensive exposure to tuberculous cattle. Calmette and Guerin attributed this resistance to reinfection, to the impregnation of the lymphatic system with viable virulent tubercle bacilli. Since the use of viable tubercle bacilli, even in minute amounts, cannot be recommended as an immunizing agent for man, Calmette and Guerin attempted to attenuate the tubercle bacillus so that it would be no longer virulent, for animals as susceptible as the guinea pig. They modified a virulent bovine strain of the tubercle bacillus, by transplanting it for 230 generations over a period of 13 years on culture medium containing beef bile. These investigators attributed the attenuation of this strain, which they designated BCG (Bacillus Calmette and Guerin), to the presence of beef bile. Our own observations as well as the observations of others, who have isolated and determined the virulence of large numbers of strains of tubercle bacilli, indicate that certain strains may lose their virulence spontaneously and rapidly on culture medium without the addition of bile. The BCG culture is avirulent for the usual laboratory animals, even in doses as large as 20 mgm. or greater. It induces allergy, retains the property of producing potent tuberculin, is antigenic, and produces local anatomical tubercles.

Since its initial use in man about 25 years ago, when it was first administered per os to newborn babies, millions of persons of all ages have received the vaccine per os, subcutaneously, intracutaneously or by means of multiple puncture. Thus far not a single, unequivocal case of tuberculosis which could be attributed to the BCG vaccine has been reported.

In the United States, Park and Kereszturi (6) in New York and Aronson and Dannenberg (7) in Philadelphia, carried out controlled studies on newborn babies to evaluate the effectiveness of BCG vaccine in reducing the mortality and morbidity from tuberculosis. The results obtained suggested that a certain degree of protection was afforded by the BCG vaccine. It is, however, difficult to carry out long range studies in urban communities, because of the transient nature of a high per cent of the population and the marked variations in economic and social conditions.

CHARACTER OF GROUPS STUDIED

Because of the high mortality and morbidity from tuberculosis noted among the Indians of the United States and Alaska, the Health Division of the Office of Indian Affairs has been interested in utilizing all available measures in controlling this disease. In 1935 the Office of Indian Affairs undertook a cooperative study with the Henry Phipps Institute, University of Pennsylvania, to determine the protective value of BCG vaccine under carefully controlled conditions. The selection of certain Indian Agencies was based on the fact that these Indians are indigenous to these areas, are non-migratory, cooperative and accessible year after year. This study was conducted among the Indians living on the Pima Agency, Arizona, the Wind River Agency, Wyoming, the Turtle Mountain Agency, North Dakota, the Rosebud Agency, South Dakota, and on non-reservation Indians living in 12 towns and villages of southeastern Alaska. While these Indians vary in their physical characteristics, dietary habits, social and cultural patterns, their economic level is uniformly low, housing poor and crowding the rule.

The Indians included in this study differ in their linguistic and racial stocks and in their cultural patterns. They represent the agricultural groups, the Indians of the plains who were historically hunters, the woodland Indian groups and the Indians of Alaska who lived on and off the sea. In their dietary habits they range from the high carbohydrate diet of the Pima Indians of Arizona, and the high protein diet of the Shoshones and Arapahoes of Wyoming and the Rosebud Sioux of South Dakota, to the rich fat diet of the Indians of southeastern Alaska. Their racial stocks vary from the relatively pure-blooded Pimas of Arizona and the Arapahoes of Wyoming to the Chippewa Indians of the Turtle Mountain Agency, North Dakota, with their marked French-Canadian admixture and the Shoshone Indians of Wyoming, admixed with French-Canadian and other white strains.

The distribution of income per family per year for the agencies studied in the United States is presented in Table 1.

It will be observed from Table 1 that the annual income per family is comparably low for those living on the Rosebud and Turtle Mountain Agencies and higher among those living on the Pima and Wind River Agencies.

TABLE 1

PER CENT DISTRIBUTION OF FAMILIES BY AMOUNT OF FAMILY INCOME AND BY AGENCY FOR 1942

AGENCY	UNDER $200	$200–499	$500–749	$750–999	$1000–1499	$1500–2000	$2000 & OVER
Pima	13.0	39.65	17.78	10.91	9.95	5.47	3.29
Rosebud	4.85	75.75	12.25	5.04	1.41	0.57	0.11
Turtle Mt.	5.00	78.30	19.90	5.0	1.00	0.50	0.30
Wind River	3.49	14.42	9.55	14.18	16.72	19.05	22.55

OCCURRENCE OF TUBERCULOSIS

Before evaluating the role of BCG vaccine in the control of tuberculosis it was essential to determine, among the general population of each area, the incidence of tuberculous infection and the morbidity and mortality from this disease. These data serve as an index of the intensity of exposure to which those included in this study might be subjected.

The incidence of tuberculous infection was determined by means of the intracutaneous tuberculin test. An initial dose of 0.00002 mgm. of a preparation of tuberculin PPD, prepared by Dr. Florence Seibert of the Henry Phipps Institute, Philadelphia, was used. Those who failed to react to this amount 48 hours later were reinjected with 0.005 mgm. of the same tuberculin and a final reading was made after another 48 hours. All children attending school were tested, as well as a signifi-

cant per cent of unselected preschool age children and a small per cent of the older age groups. It was not considered essential to attempt to test a larger per cent of the older age groups when sampling indicated that practically one hundred per cent reacted to tuberculin. The results of the tuberculin tests among the general population are presented in Table 2 and are compared with the results of tuberculin surveys conducted under similar conditions among white persons living in rural areas of Michigan and Minnesota and among colored persons living in rural areas of the south.

These surveys indicate that the incidence of tuberculous infection among the Indians in the areas tested rises rapidly with increasing age, exceeding that noted among the colored persons residing in rural areas of the south and among white persons residing in rural areas of Michigan and Minnesota. Among Indians as among colored there is a marked sensitivity to tuberculin, in all probability due to intensity of exposure. Of the Indians tuberculin tested, 91.4 per cent reacted to the dose of 0.00002 mgm. of tuberculin PPD and of these 55.2 per cent had a local inflammatory reaction exceeding 20 mm. in diameter (3+), associated in a small per cent of cases with a systemic reaction.

The amount of tuberculous infection varies in different agencies, as is shown in Table 3. It was highest among those under five years of age on the Rosebud Agency, South Dakota, and reached 100 per cent in the 20 to 24 year group tested there. The lowest incidence of

TABLE 2

TUBERCULIN REACTION BY AGE AND RACE IN CERTAIN AREAS OF THE UNITED STATES AND ALASKA

AGE IN 5 YEAR PERIODS	INDIAN POPULATION		WHITE		WHITE		COLORED	
	United States and Alaska		Rural Michigan		Rural Minnesota		Rural South	
	Number tested	Per cent positive	Number tested	Per cent positive	Number tested	Per cent positive	Number tested	Per cent positive
Under 5	1276	12.7	261	6.1	—	—	770	15.7
5 to 9	2267	35.3	2573	9.6	276	9.4	2095	30.1
10 to 14	2118	61.6	3133	17.8	389	20.3	2435	50.0
15 to 19	1240	83.5	1069	26.4	182	40.6	1660	70.3
20 to 24	374	90.9	234	41.0	—	—	1101	78.1
25 to 29	235	97.4	206	52.4	—	—	721	81.7
30 to 34	178	96.6	160	54.4	—	—	560	83.6
35 to 39	160	98.8	147	72.1	—	—	527	85.7

TABLE 3

INCIDENCE OF TUBERCULIN REACTION BY INDIAN AGENCY AND BY AGE

Age in 5 Year Periods

AGENCY	UNDER 5		5 TO 9		10 TO 14		15 TO 19		20 TO 24	
	Number tested	Per cent positive	Number tested	Per cent positive	Number tested	Per cent positive	Number tested	Per cent positive	Number tested	Per cent positive
Pima	410	11.4	628	23.0	478	48.5	259	77.2	136	89.7
Wind River:										
Shoshone	81	6.2	103	24.2	92	56.5	59	83.1	46	71.7
Arapaho	127	7.0	122	42.6	115	70.4	82	85.4	41	97.5
Rosebud	100	25.0	582	45.9	721	65.6	409	84.6	14	100.0
Turtle Mountain	—	—	100	38.0	120	71.6	296	91.2	128	90.6
Alaska	533	14.2	609	39.5	453	67.1	116	71.5	9	100.0

tuberculous infection was noted among the Shoshone Indians of the Wind River Agency, Wyoming. There the incidence of infection was 6 per cent for those under 5 years of age, while in the 20 to 24 year age group the incidence was 72 per cent.

TABLE 4
PER CENT SIGNIFICANT PULMONARY TUBERCULOUS LESIONS BY AGENCY

AGENCY	TOTAL POPULATION	EXAMINED ROENTGENOLOGICALLY		TUBERCULOUS LESIONS
		Number	Per cent	Per cent
Rosebud	7994	2450	30.6	3.1
Wind River Shoshone	1026	574	55.9	5.7
Arapaho	1164	740	63.6	5.8
Pima	4841	2060	42.5	1.1
Alaska	5000	3897	77.6	6.9

Roentgenological examination of the chest was made of an unselected significant sample of the general population in each area to determine the incidence of significant pulmonary lesions characteristic of tuberculosis. It will be noted from Table 4 that the per cent of the general population examined roentgenologically varied, but was sign ficant statistically. The highest incidence of pulmonary lesions was found in southeastern Alaska, where the morbidity and mortality from tuberculosis has long been known to be high.

Since the mortality rate from tuberculosis reflects the incidence of clinically manifest cases of this disease in the ratio of approximately nine cases for each death, it can be used as a measure of the extent and intensity of possible exposure in a community. This information was compiled from the available agency records for the different years, and is summarized in Table 5.

The foregoing data indicate, in as objective a manner as possible, the low economic condition prevalent among the Indians of the agencies studied, the high incidence of tuberculous infection and the high morbidity and mortality from tuberculosis. It was under these conditions that the effectiveness of BCG vaccine in controlling tuberculosis was to be determined.

TABLE 5
DEATH RATE PER 100,000 ALL CAUSES AND FROM TUBERCULOSIS BY AGENCY AND YEAR

YEAR	WIND RIVER AGENCY			ROSEBUD AGENCY			PIMA AGENCY			TURTLE MOUNTAIN AGENCY		
	Total population	Death rate per 100,000		Total population	Death rate per 100,000		Total population	Death rate per 100,000		Total population	Death rate per 100,000	
		All causes	Tuberculosis		All causes	Tuberculosis		All causes	Tuberculosis		All causes	Tuberculosis
1935	1979	2375	657	—	—	—	5866	2727	442	—	—	—
1936	2033	2607	383	—	—	—	5908	2353	237	—	—	—
1937	2104	3660	618	—	—	—	5854	2425	307	—	—	—
1938	2121	2688	377	7921	2171	520	5993	1836	200	—	—	—
1939	2190	2009	365	7994	1801	400	6094	1936	164	3287	2038	304
1940	2230	2511	493	8070	1425	259	6093	1428	148	3419	1180	292
1941	2289	2780	165	8127	1279	443	6236	1750	229	3483	1610	373
1942	2348	2044	426	8203	1413	280	6399	1750	172	3572	672	54
1943	2262	1680	221	8279	1920	398	6479	1394	108	—	—	—
1944	2334	2785	257	8355	1627	323	6632	1598	286	3738	803	0
1945	2376	1851	210	8532	1289	363	6745	1823	89	3845	806	78
1946	2438	1558	246	—	—	—	6745	1734	133	—	—	—

PROCEDURE

We assume that a positive tuberculin reaction, with the amounts of tuberculin PPD used in this study, is in the vast majority of cases the specific allergic response resulting from tuberculous infection. It is generally

agreed that such a reaction indicates resistance to reinfection and the use of BCG vaccine or other specific immunizing agents is therefore not indicated, in those who react to tuberculin. On the other hand, specific immunization with BCG vaccine is indicated in those who have escaped infection and who therefore fail to react to tuberculin. Such treatment results in the production of a self-limited primary local lesion, followed by specific allergy as measured by the tuberculin reaction. To what degree this vaccination protects against tuberculous reinfection was to be determined.

To eliminate or minimize any bias in the selection of cases for this study, all children attending the Indian Service day schools and the denominational boarding schools, and as many children of preschool age as possible, were tested with tuberculin PPD. A total of 3008 persons, ranging in age from less than one year to 20 years, living on the different agencies and in southeastern Alaska, and who failed to react to the intracutaneous injection of 0.00002 and 0.005 mgm. of PPD or who gave a doubtful reaction with 0.005 mgm. of PPD were selected for this study.

TABLE 6
DISTRIBUTION BY AGE OF BCG VACCINATED AND CONTROLS

AGE IN 5 YEAR PERIODS*	NUMBER		PER CENT	
	Vaccinated	Control	Vaccinated	Control
Under 5	433	414	27.9	28.4
5 to 9	661	623	42.6	42.7
10 to 14	385	351	24.8	24.1
15 to 20	72	69	4.7	4.8
Total.....	1551	1457		

* Attained age at beginning of study.

The value of any controlled study depends to a great degree upon the equality of the samples. The groups studied must be comparable and the selection of members of these groups made without bias. To meet these requirements a card was prepared for each person who failed to react to tuberculin. All of these cards were sorted by sex and by year of birth for each school and adjacent district. An alternate division of the cards was then made within each sex and age group. Approximately one half received the BCG vaccine, while the remaining number served as controls. In a small number of instances the person selected for vaccination was absent from school, and one of those listed for the control group was substituted and the absentee served as control. The comparability of the two groups by age is shown in Table 6.

This study was initiated at the Pima Agency, Arizona, in December 1935 and was extended in 1936 to include the Shoshone and Arapaho Indians living on the Wind River Agency, Wyoming, the Chippewa Indians of the Turtle Mountain Agency, North Dakota. In 1937 and 1938 the Sioux Indians of the Rosebud Agency, South Dakota, and the Indians of southeastern Alaska were included in the study as well as a second series at the Pima Agency, Arizona. The 1551 persons selected for vaccination were injected with one of 13 different lots of vaccine prepared locally at each agency in a mobile laboratory. The BCG vaccine was prepared from cultures of the organism grown on Sauton's synthetic medium for various periods from 7 to 30 days. The culture was collected, the excess fluid removed and the moist bacillary mass weighed and suspended in sterile physiological saline. Those selected for vaccination received an intracutaneous injection of 0.1 cc. of the vaccine containing either 0.1 or 0.15 mgm. of the moist culture. The injection was made as superficially as possible in the skin over the deltoid region. The vaccine was used within the first three days of its preparation and in most instances within 1 day after preparation. At the same time, the control group received an intracutaneous injection of 0.1 cc. physiological saline. Those included in this study were not isolated either before or after vaccination, nor was their mode of living modified.

The intracutaneous injection of the vaccine was followed, 48 hours later, by the appearance of a sharply defined nodule measuring approximately 4 mm. in diameter and 1 mm. in

height. During the first two weeks after vaccination, the nodule decreased somewhat in size and was followed by a rapid increase in size of the nodule 3 to 4 weeks after the injection. At this time many of the nodules had a doughy consistence. Ulceration occurred by the 4th week in about 75 per cent of the cases, and persisted for from 4 to 8 weeks. In a high per cent of the cases there was noted a sense of fullness in the axilla of the vaccinated side and in approximately 5 per cent of the cases the regional lymph nodes along the anterior axillary fold were palpable. In no instance did the lymph nodes ulcerate nor did the local ulcer require any surgical treatment. Healing of the local ulcer was completed in approximately 12 weeks after vaccination, leaving a soft scar measuring from 5 to 10 mm. in diameter, which has persisted for the 11 years of this study.

Smears prepared from the local ulcers at varying periods of time showed at first numerous polymorphonuclear cells, numerous clumps of extracellular acid-fast bacilli, as well as acid-fast bacilli phagocyted within large mononuclear cells. Later there was noted a significant increase in the number of lymphocytes and decreasing numbers of acid-fast bacilli. At first the acid-fast bacilli stained deeply and more or less uniformly, but with increasing time they stained less intensely and appeared more granular. Fibrin appeared later and the acid-fast bacilli disappeared or were found only after a long search.

The possibility that a few of the tuberculin-negative cases had undergone a tuberculous infection, but were in a pre-allergic state at the time that the tuberculin test was carried out, had to be given consideration. To control this possibility, the site of injection of all BCG vaccinated persons was re-examined 48 hours after the injection. In all there were observed 7 cases who, 48 hours after the injection of the vaccine, showed an acute local inflammatory reaction (Koch phenomenon). In 5 instances this was due to injection, by error, of tuberculin positive cases, while in 2 instances the individuals were tuberculin-negative, but were evidently in the pre-allergic phase at the time of testing. It is of interest that these 2 cases, which have since died from tuberculosis, are among the 6 tuberculosis cases terminating fatally among the vaccinated during the course of this study.

Of the 3008 persons included in this study, approximately 85 per cent were given a roentgenological examination of the chest at approximately the same time the tuberculin test was carried out, or as soon after as possible.

Re-examinations of the BCG vaccinated and control groups were carried out at approximately annual intervals and as many of the persons as could be located were tuberculin tested and X-rayed. If absent from the agency, efforts were made to determine their whereabouts and whether they were alive or dead.

EVALUATION OF RESULTS

The significance of the results obtained in this study depends upon the similarity of the vaccinated and control groups, upon the comparability of the per cent re-examined and whether or not both groups experienced the same frequency and degree of exposure to manifest cases of tuberculosis. The comparability of both groups in age distribution has been pointed out in Table 6. The number re-examined by means of the tuberculin test and roentgenologically, represents a high percentage of those in the study and, as is indicated in Table 7, is almost identical for both groups in any given year. The reduction and variations in the number re-examined after the sixth year are due to World War II when field work was necessarily curtailed and certain agencies were not visited. In June, 1944, field work was discontinued, and at that time all of those in the study had had a minimum of 6 annual examinations. In some areas 7 annual examinations had been made, and in one agency 8 examinations had been carried out. In September, 1946, field work was resumed, and all of the areas were visited during 1946–1947. At that time the tuberculin tests and roentgenological examinations

were made in two areas for the 9th year after the initiation of the study and for the 10th and 11th years in the remaining areas. Consequently, the per cent of persons re-examined following the sixth annual examination is based on the original number of cases in the areas visited and not on the original total of all areas.

A measure of the effectiveness of BCG vaccine in controlling tuberculosis depends upon whether both groups experience the same degree and frequency of exposure to tuberculosis. In a previous analysis of the results of the first six years of this study (8) directed by Dr. Carroll Palmer, Tuberculosis Control Division of the United States Public Health Service, it was found that approximately 20 per cent of both groups were exposed to tuberculous infection, and that the degree of contact was essentially the same for both groups. These findings, however, were based on domiciliary sources of infection only. It has been our observation over a period of years that manifest cases of tuberculosis roam at will throughout the agencies and adjacent communities, where they frequently attend public meetings, games, and frequently visit other homes for varying periods of time. If hospitalized, they remain in the sanatorium only a short time. Those who are bedridden are often visited by neighbors and friends. These extra-domiciliary sources of infection, while not measurable directly, are significant.

TABLE 7

PERCENTAGE OF LIVING PERSONS IN STUDY RE-EXAMINED

YEARS AFTER VACCINATION	TUBERCULIN TESTED				X-RAYED			
	Vaccinated		Control		Vaccinated		Control	
	Original number	Per cent retested	Original number	Per cent retested	Original number	Per cent retested	Original number	Per cent retested
1	1551	96.4	1457	90.4	1551	97.4	1457	96.8
2	1551	94.5	1457	93.7	1551	96.8	1457	96.4
3	1551	94.9	1457	95.4	1551	96.1	1457	96.5
4	1551	95.2	1457	92.9	1551	95.9	1457	93.9
5	1551	89.7	1457	90.0	1551	91.2	1457	91.5
6	1551	80.8	1457	77.5	1551	84.1	1457	81.8
7	752	78.8	702	81.6	752	81.8	702	84.1
8	428	70.4	425	70.4	428	71.6	425	76.3
9	799	74.9	755	72.1	799	76.8	755	72.2
10	266	68.6	248	72.1	266	69.0	248	72.1
11	486	81.3	454	78.3	486	80.2	454	78.2

RESULTS

Tuberculin Reaction:

It cannot be said at this time that the question of the mechanism of immunity to tuberculosis and its relationship to allergy have been settled. It has been demonstrated that a high degree of parallelism between allergy and immunity exists, but there is also some evidence, with which we are in accord, that the two conditions do not necessarily co-exist. However, for want of a better index we are arbitrarily employing allergy, as indicated by the tuberculin reaction, as a measure of immunity.

That BCG vaccine is capable of inducing a high and persistent rate of allergy is indicated in Table 8.

It will be noted from this table that among the vaccinated a positive tuberculin reaction was present in 93.3 per cent of those tested 1 year after vaccination and that this high rate has persisted with but slight variations throughout the period of observation. Among the control group only 12.7 per cent reacted to tuberculin one year after the initial negative tuberculin reaction and the increment of

positive reactions was approximately 5 per cent for each subsequent year of observation.

The sensitivity to tuberculin induced by BCG vaccine is not as marked as that resulting from natural infection. This is indicated by the smaller per cent of the vaccinated who react to 0.00002 mgm. of tuberculin PPD and the fact that the degree of the local reaction is less severe than that noted among the controls. With increasing time the intensity of the tuberculin reaction also increased among the vaccinated. This suggests that among the vaccinated as among the controls natural infection with virulent tubercle bacilli has occurred.

TABLE 8

Frequency of Tuberculin Reaction by Dose and Year of Observation in Vaccinated and Controls

Years after vaccination	Vaccinated				Controls			
	Original number	Per cent positive to PPD			Original number	Per cent positive to PPD		
		0.00002 mgm.	0.005 mgm.	Total		0.00002 mgm.	0.005 mgm.	Total
1	1551	36.7	56.6	93.3	1457	7.3	5.4	12.7
2	1551	47.6	45.7	93.3	1457	13.5	5.1	18.6
3	1551	54.5	38.0	92.5	1457	17.5	7.1	24.6
4	1551	53.3	38.9	92.2	1457	22.7	7.6	30.3
5	1551	54.9	36.8	91.7	1457	27.9	7.2	35.1
6	1551	61.2	31.0	92.2	1457	33.0	9.3	42.3
7	752	58.0	36.9	94.9	702	26.8	11.4	38.2
8	428	54.0	40.9	94.9	425	25.3	14.7	40.0
9	799	76.7	15.6	92.3	755	52.0	3.0	55.0
10	266	61.7	25.8	87.5	248	26.3	11.7	38.0
11	486	61.4	28.8	90.2	454	35.5	6.2	41.7

Mortality:

The most important evidence of the efficacy of the BCG vaccine is brought out when a comparison is made of the total mortality rates and of the mortality and morbidity rates from tuberculosis in the vaccinated and control groups. The results of such a comparison are significant and definite and do not lend themselves to misinterpretation. Among the vaccinated a total of 55 persons died during the period of this study, which varied, as has previously been stated, from 9 to 11 years on the different agencies. During this same period of time 109 of the controls have died. The BCG vaccinated group experienced a total of 16,406 years of observation and in terms of death per 1000 person-years yielded a rate of 3.1. The control group experienced a total of 15,207 years of observation and the rate per 1000 person-years of observation was 7.2. These rates when compared with the rates of 3.8 and 7.2 per 1000 person-years for the vaccinated and control groups respectively noted at the end of the first 6 years of observation (8) indicate that the ratio of deaths in the two groups has remained almost constant.

When the death rate from tuberculosis is compared in the two groups the differences are even more striking. In the BCG vaccinated group 6 have died from tuberculosis, since the beginning of the study, while among the controls 53 have died from this disease. In terms of mortality rate per 1000 years of observation the rate from tuberculosis for the vaccinated is 0.4, while for the controls it is 3.5. Of the 6 deaths from tuberculosis which occurred among the vaccinated 2 occurred in persons who had had a Koch phenomenon following vaccination. A third death from tuberculosis occurred in a child who failed to react to tuberculin one year after vaccination.

Table 9 presents a comparison of the mortality from tuberculosis and from other causes by 5 year age periods, for the vaccinated and control groups.

The number of deaths from tuberculosis among the vaccinated is too small to permit drawing any conclusions as to effect of age or sex on the development of tuberculosis. Among the control group, on the other hand, the number of deaths from tuberculosis is significant in each age period, except for the 25 to 29 year age group, where the number of person-years of observation is small. It will be noted that the mortality rate from tuberculosis rises sharply in the age group of 15 to 19 and 20 to 24. Not only does age modify the occurrence of fatal tuberculosis but sex seems to play an important role. Of the 6 deaths from tuberculosis which occurred among the vaccinated 4 were females and 2 males. Among the controls, as indicated in Table 10, fatal tuberculosis occurs almost twice as frequently among the females as among the males.

TABLE 9

MORTALITY RATES, TUBERCULOUS AND NON-TUBERCULOUS, IN VACCINATED AND CONTROLS BY AGE GROUPS

AGE IN 5 YEAR PERIODS	VACCINATED					CONTROLS				
	Number of person-years of observation	Deaths—tuberculosis		Deaths—other causes		Number of person-years of observation	Deaths—tuberculosis		Deaths—other causes	
		Number	Rate per 1000 person-years	Number	Rate per 1000 person-years		Number	Rate per 1000 person-years	Number	Rate per 1000 person-years
0–4	1327	1	0.7	11	8.3	1303	2	1.5	11	8.4
5–9	4037	0	—	7	1.7	3757	6	1.6	12	3.2
10–14	5595	4	0.7	9	1.6	5170	13	2.5	9	1.7
15–19	3998	1	0.3	14	3.5	3667	22	6.0	13	3.6
20–24	1311	0	—	7	5.3	1179	10	8.5	9	8.1
25–29	138	0	—	1	7.3	131	0	—	2	15.3
All ages.....	16406	6	0.4	49	3.0	15207	53	3.5	56	3.7

Morbidity:

Despite the fact that the interpretation of roentgenograms cannot as yet be considered entirely objective in nature, they do offer at this time the best medium for determining the occurrence and nature of pulmonary lesions. It is unfortunate that at this time it has not been possible to review the complete files of those cases which show doubtful or indefinite pulmonary lesions and for the time being these will be reported as lesions of doubtful etiology. Pending further study of the X-ray films we have made a review of all roentgenological reports of our cases. This analysis indicates that among the vaccinated there have occurred 19 cases of primary tuberculosis, while among the controls 97 were so diagnosed. Parenchymal tuberculous lesions and miliary tuberculosis were observed in a total of 16 instances among the vaccinated and in 59 of the controls. Pleural effusion and evidence of pleuritis was noted in 43 of the vaccinated and in 37 of the controls.

EFFECTIVENESS OF BCG VACCINE IN NEWBORN CHILDREN

The evaluation of BCG vaccine in controlling tuberculosis in a general population of varying ages requires observation over a long period of time. Because of the relatively high mortality from tuberculosis in the first three years of life, it was believed that a more rapid determination of the efficacy of BCG vaccine in controlling tuberculosis could be made by following a group of newborn chil-

dren for approximately five years. For the purpose of this supplementary study, children born in the hospital of the Turtle Mountain Agency, North Dakota and those born in the hospital of the Rosebud Agency, South Dakota were selected. The original plan was to vaccinate alternate cases in each hospital. Unfortunately in one of these hospitals this plan was not followed and the newborn children were vaccinated more or less at random. Between December 1938 and December 1940, 123 newborn babies were vaccinated intracutaneously with 0.1 mgm. of BCG vaccine within several days after birth. The BCG vaccine was prepared at the Henry Phipps Institute, Philadelphia and flown from there to each agency. During the same period of time 139 newborn babies were untreated and served as controls. The newborn babies returned home with their mothers and no changes were made in the home surroundings or mode of living. These babies, like those in the initial study, were tuberculin tested and X-rayed annually, except for an interval during the war, when certain activities had to be curtailed. At the time of the first examination these children ranged in age from 3 to 14 months. Eighty-five per cent of the vaccinated and 77 per cent of the controls were tuberculin tested and 95 per cent of both groups were examined roentgenologically. Ninety-one per cent of the vaccinated and 3.7 per cent of the controls reacted to tuberculin. Roentgenological examination at the same time revealed one case of primary tuberculosis in a control. This child died 1 month later from tuberculous meningitis.

In 1946 when this "newborn" group ranged in age from 6 to 8 years, 82 per cent of each of the vaccinated and controls were retested with tuberculin, while 83 per cent of the vaccinated and 78 per cent of the controls were examined roentgenologically. Among the vaccinated the tuberculin reaction was positive in 80 per cent of those tested, a decrease of 11 per cent from the tuberculin results observed one year after vaccination. Among the controls the tuberculin reaction had increased from the 3.7 per cent noted during the first year of life to 26.5 per cent.

During the entire period of observation, which ranged from 6 to 8 years, 7 of the vaccinated cases have died and none from tuberculosis. Among the controls, during the same period of time, 15 have died from all causes. Four of these died from tuberculosis and all four died within the first three years of life.

A review of all roentgenological reports of this series of "newborn" cases shows that among the vaccinated primary tuberculosis has developed in 4 children. Among the control groups during the same period of time

TABLE 10

MORTALITY RATES, TUBERCULOUS AND NON-TUBERCULOUS, BY SEX AND AGE GROUP AMONG CONTROLS

AGE IN 5 YEAR PERIODS	MALE					FEMALE				
	Number of person-years of observation	Deaths—tuberculosis		Deaths—other causes		Number of person-years of observation	Deaths—tuberculosis		Deaths—other causes	
		Number	Rate per 1000 person-years	Number	Rate per 1000 person-years		Number	Rate per 1000 person-years	Number	Rate per 1000 person-years
0–4	684	2	2.9	4	5.8	619	0	—	7	11.6
5–9	1946	2	1.0	8	4.1	1811	4	2.2	4	2.2
10–14	2594	2	0.8	5	1.9	2491	11	4.4	4	1.6
15–19	1855	8	4.3	6	3.2	1812	14	7.7	7	3.8
20–24	559	5	8.9	6	10.7	624	5	8.0	3	4.8
25–29	64	0	—	0	—	67	0	—	2	30.0
All ages.....	7702	19	2.5	29	3.8	7424	34	4.6	27	3.7

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11 cases of primary tuberculosis have occurred, including one who developed fatal progressive pulmonary tuberculosis, and one tuberculous meningitis. In addition to these two deaths, two others died from tuberculous meningitis without showing at the time of the last examination any pulmonary involvement.

DISCUSSION

Although BCG vaccine has been used in man for the past 25 years, its use has not received universal acceptance. The original objection to the use of viable attenuated organisms was, of course, the fear that the culture might revert and become virulent. This objection has not proved valid, for up to the present time no one has succeeded in increasing the virulence of the BCG culture, nor is there evidence that the virulence of any strain of tubercle bacillus can be increased by available laboratory procedures. The best proof of the innocuousness of the BCG vaccine is the fact that it has been administered by various routes, in varying amounts, to millions of persons throughout the world, and no single case of clinical tuberculosis can be traced to this culture.

Another and more significant objection has been based on the fact that in spite of the large number of investigations dealing with the use of BCG vaccine and the millions vaccinated, no large scale study had been made under properly controlled conditions. The results originally claimed for its protective value in man were not confirmed by critical statistical analysis. The controlled study here reviewed was planned in the hope of answering some of these questions and of meeting objections with valid data.

The most recent objection raised against the widespread use of BCG vaccine has been on the basis that the resulting tuberculin reaction, due to BCG vaccine, would mask and confuse the significance of tuberculin reactions resulting from spontaneous infection, thus making it more difficult to detect sources of tuberculous infection. This objection might be given more consideration when the occurrence of tuberculosis in man approaches the low rate which is now found among cattle in the United States. This objection cannot be considered a valid one as long as there exist areas in the world with death rates of 300 per 100,000 and higher.

The results of this study indicate that the use of BCG vaccine, as a method of controlling tuberculosis, is a practical and safe procedure. Observations for as long as 11 years indicate that the persons vaccinated compared with the controls show a persistent allergy and resistance to tuberculosis. Opinions may vary as to the advisability of the universal use of the BCG vaccine. In areas where the tuberculosis rate is high, living conditions poor and hospital facilities inadequate for the care of manifest cases, the use of BCG vaccine is indicated. On the other hand, where the death rate from tuberculosis is low and is falling, where homes are widely scattered, housing and hospital facilities adequate, the widespread use of this vaccine in the general population is questionable. BCG vaccination is indicated for tuberculin negative medical students and nurses, hospital personnel, and military personnel assigned to duties in areas with a high tuberculosis rate. The use of BCG vaccine as an immunizing agent against tuberculosis should serve as an auxiliary weapon in the control of this disease and must not be looked upon as the solution of the tuberculosis control problem.

SUMMARY

1. The value of BCG vaccine in increasing resistance to tuberculosis has been investigated among some Indians of the United States and Alaska.

2. Freshly prepared BCG vaccine was administered intracutaneously to 1551 American Indians ranging in age from less than 1 year to 20 years, and to 123 newborn babies. At the same time 1457 Indians of comparable age and living under comparable conditions received an intracutaneous injection of sterile physiological salt solution and served as con-

trols, as did 139 newborn children who also served as controls.

3. No untoward local or general reaction followed the injection of the vaccine and in no instance was surgical intervention necessary.

4. By means of the tuberculin test and roentgenogram of the chest both vaccinated and controls were followed over a period of from 9 to 11 years, while the newborn children were followed for from 6 to 8 years.

5. The vaccinated cases were observed for a total of 16,406 person-years, and the controls for 15,207. The mortality rate from all causes among the vaccinated was 3.1 per 1000 years of observation and 7.2 for the controls. Six deaths from tuberculosis occurred among the vaccinated and 53 among the controls yielding mortality rates of 0.4 and 3.5 per 1000 years of observation for this disease respectively. The death rates from non-tuberculous causes were 3.0 and 3.7 per 1000 person-years of observation for the vaccinated and controls respectively.

6. Among the controls the death rate from tuberculosis was highest in the 15 to 19 and 20 to 24 year age groups and was approximately twice as high among the females as among the males.

7. Among the newborn children observed for from 6 to 8 years, 7 of the vaccinated have died but none from tuberculosis. Among the controls 15 deaths have occurred, 4 of them from tuberculosis.

8. The tuberculin reaction which was positive in 93.3 per cent of the vaccinated one year after vaccination has remained at approximately the same level, throughout the course of this study, and after 11 years of observation 90.2 per cent of the living were tuberculin positive. Among the controls one year after the initial negative tuberculin test 12.7 per cent became positive, and there has been a gradual increase in the per cent of the controls who have reacted to tuberculin.

The invaluable assistance at all times of Miss Erma Parr of the Tuberculosis Control Division, the U. S. Public Health Service, is acknowledged. To Mrs. Mabel Head, Pima Agency, Arizona, and to Miss Ruth Holtzworth of the Turtle Mountain Agency, South Dakota, public health nurses of the Health Division, Office of Indian Affairs, we are greatly indebted for their wholehearted cooperation and interest displayed during the many years of this study.

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Psychosomatic Principles and Patterns in Disorders of the Special Senses*

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I FEEL signally honored to have been chosen to give a Weir Mitchell lecture, and also humble and a bit fearful that I shall fail to meet and maintain the standards set by those lecturers who have preceeded me in these undertakings to bring the memory and particularly the outstanding accomplishments of this great man to the attention of new generations of physicians and scientists.

It is not my intention tonight to review the interesting life history of Dr. Mitchell. It has been done a number of times by others better qualified for the task, but in as much as one of his early special interests had something to do with the selection of the topic for this evening I should like to remind you that S. Weir Mitchell (1830–1914) although more widely known as a neurologist, poet and novelist made worthful contributions to American physiology and stimulated a lot of activity in that field after his period of study with the famous French physiologist Claude Bernard.

He was an original thinker and worker. Among other accomplishments he was the first to describe causalgia in 1864, post paralytic chorea in 1874, and with William Thomson he first recognized the relationship between eyestrain and a variety of headache. In 1878 he described erythromelalgia (Weir Mitchell's Disease), a rare vasomotor neurosis of the extremities (Am. J. Med. Sci. 1878, LXXXVI, 1). The term causalgia means "burning pain" that is sometimes present in injuries of the major peripheral nerves. It constitutes a syndrome resulting from war wounds. The burning pain is associated with hyperaesthesia and trophic alterations in the tissues of the affected extremity. During the Civil War he had a special ward in the Military Hospital of Philadelphia where, with Morehouse and Keen, he made intensive studies of the peripheral nerves which were published later (1872) in a book entitled "Injuries of Nerves and Their Consequences".

These less known early interests in sensorymotor phenomena and his universally well known command of the field of the functional neuroses as they were understood in his day has stimulated me to present some material on the psychosomatic aspects of the special senses, a modest portion of which has not heretofore appeared in the literature, as far as I am informed.

To introduce the subject one may emphasize that biologically the first concern of any individual is to continue to survive in his particular environment, in other words to adapt to conditions. Numerous mechanisms have developed to accomplish this purpose, but in the biologic organization of the body complexes there are phylogenetically and ontogenetically two master interlocked integrating systems of tissues and organs, namely the nervous system and the circulatory system. Although several other organ constellations of functions are in vital positions as far as the maintenance of life and its economy are concerned, the activity of the organism in the aggregate depends constantly upon the integrity of these two great systems. As the mind represents the total activity of the organism it is accepted generally that one should expect to find emotional and sometimes intellectual dysfunctions associated with structural and physiological alterations in the various organs of the body.

Modern biology has obliterated fixed lines.

* S. Weir Mitchell Oration X, The College of Physicians of Philadelphia, 7 January 1948.

The psychic aspects of an individual are also functioning processes which under proper conditions are convertible into certain physical ones.

Sensation, which is our main focus of attention for tonight, is the response of a particular area of the organism to the first impacts of the freshly stimulated "points". A long continued permanence in the relation of points (moments) results in structuralization of sensory zones and organs.

It is a recognized fact that bodily organs have many personal and social meanings for patients and even for normal persons, and have become a special division of our very language. That is, there is an "organ language" common to all peoples, and I shall enumerate some of the characteristics:

1. Organ analogies are exceedingly common in daily speech, e.g.: "He has guts"; "She has nerve"; One is "soft" or "hard" hearted; "He has no back bone—is spineless"; He is "stiff necked"; "I cannot stomach that"; or, "I can't swallow such an idea".

2. Healthy organs may become endowed with a supposed malfunction or with odd sensations that dominate the individual's existence constituting a disproportionate importance in the framework of health and disease.

3. Organs may become prominent as symbols of a sexual or of a social nature. (We frequently say of one who uses vulgar or improper language that he has a "dirty mouth", and some small children are the recipients of an accompanying symbolic act on the part of a parent who "purifies" the offending part with soap.)

4. Organs are of social significance particularly when they are involved in such matters as sterility or are unsightly as in strabismus or carry moral implications such as venereal diseases. Even cancer of some organs is still not mentioned freely in our present culture.

For the past 10 years the term psychosomatic medicine has represented an attitude that has stimulated and encouraged workers to gain much valuable knowledge about the human organism. In the total picture of an illness there are at least three groups of factors that have to be considered. First, the type of individual involved from the standpoint of constitutional predispositional elements including the nature of the personality which has such an important bearing on the success of therapy. Second, the factors or combination of events that have precipitated and are perpetuating the pathological reaction, and third, the actual nature of the reaction, i.e. the phenomenology. In what zone does the principal pathology manifest itself? Actual lesions represent or are the result of an energy constellation in disease, they function in the role of a maximum focus for the energy discharge. The main discharge of energy is indicated in the critical symptom. This same law holds also for mental symptoms.

As pathologists and physicians we know that some types of lesions are permanent affairs in terms of alteration in structure and disturbance of function. In a similar fashion for example there are some forms of anxiety that seem to be "frozen" into the very structure of the person's life, and I might add that this also practically always makes for therapeutic failure in psychotherapy.

The libido or basic life force or whatever term one prefers to use for this energy is physiologic in the inclusive sense of the concept. Desires are always rooted in the soma and have some relationship with the brain, its extensions, and the regulative activities of the endocrine organs. Wishes, instinctive trends, feelings of inferiority and of superiority are all related to the body structure, and the body structure and physiology are always important in libido manifestations and in some way determine them—also every emotion has its effect upon the whole body.

There are a certain number of ways in which the individual adjusts or attempts to resolve either successfully or unsuccessfully the primary instinctive cravings that develop in every one and have to be fitted into the life plan. The following possibilities are outlined.

TABLE OF POSSIBLE END RESULTS

PRIMARY INSTINCTIVE (INFANTILE) CRAVINGS

I. *Successful adjustment to the demands of culture ("normal" or "average")*

- a. By renunciation
- b. By "drainage" into acceptable channels
- c. By identification
- d. By construction of an ideal

II. *Becoming a misfit through maladaptation*

- a. By a stronger development of the impulses
  1. Stable, permanent "wrong doing" life plan
  2. Displacement of cravings
  3. Becoming over compensated
  4. Breaking through of symptoms
- b. Pathological displacement
  1. Stronger development arrested
  2. Breaking through of symptoms
  3. Stable but active
  4. Permanent symptom formation
  5. Becoming over compensated

The individual in struggling to adapt himself often seems to cling tenaciously to the symptoms which he has developed, and which are interpreted as an attempted flight from reality into illness. It constitutes a special way of dealing with difficulties. Dr. Earl Bond has called this the "wish to fall ill". The customary use of the term "reality" has always worried me particularly the concept of "reality" vs. "unreality" in as much as all aspects of a situation are "real". Any type of experience is "real". The differences consist in the fact that there are categories of reality. One living entirely in fantasy is in one category of reality which differs from that comprising immediate current events shared by others. As far as the individual is concerned the only "unreality" possible would be a complete "blackout" or total unconsciousness.

Psychosomatic situations or manifestations arrange themselves into a number of different clinical and dynamic patterns. The most commonly seen are:

1. Physiologic tensions and mild organ dysfunctions accompanying emotional states. Often these are enhanced by the self scrutiny they encourage. One may even say that self contemplation as a mere theoretical exercise or act is definitely valid evidence of a pathological trend or attitude.

2. Conversion phenomena or a substitution for an emotional state that is not expressed through the usual normal channels.

3. Symptom organization with fairly clear cut symbolic meaning.

4. Emotion "taking advantage" of an acute physical illness from accident, operation or infectious disease to prolong convalescence and producing invalidism.

5. Organic disease per se often appears to produce a neurosis, but what actually happens is probably a breaking down of the person's defense mechanisms so that the predisposition, the personality structure and the immediate problem allows the mental disorder to develop as another attempt at adaptation.

These different clinical pictures or syndromes are encountered throughout the whole field of medicine, but it is not our purpose to even attempt to make a brief review of such a vast realm nor can we include at this time a discussion of the many psychosomatic disorders of the organs of sense, some of which have a number of physiological and medical aspects other than their special sensory function, but we shall confine our remarks to psychosomatic disorders of this function of sensation, affording more attention to some senses than others not only because it has been my good fortune to have observed some rather rare but psychologically enlightening case material, but also, the list of special senses is by no means a brief one. It includes (1) sight, (2) hearing, (3) taste, (4) smell, (5) touch, pain and temperature (skin and mucous membranes), (6) kinesthetic (muscles and synovial membranes), and (7) visceral (hunger, thirst, sex).

The sense organs are anatomical extensions of the brain by means of which it comes into contact with the rest of the world. The brain has been referred to many times as an optic ganglion (note the prominence of the eyes in

embryos). Linguistic symbols constantly refer to the mind-eye relationship, e.g., to say "I see" means, "I understand"; "Can't you see that"—"I can never see it that way", are phrases heard daily. To "see" is to know. Imagery is the sum total of our mental world.

For many years medical literature has been well infiltrated with accounts of hysterical amaurosis, amblyopia and allied ocular manifestations of psychic origin. Unilateral or bilateral hysterical restrictions of the visual field as well as other disorders of sight are all relatively common occurrences. Disorders of color sense in which red persists longest in the vision may be so extensive that it is the only color remaining. Micropsia and megalopia, painful accommodation and many varieties of pupillary conditions have been described in the hysterical type of photophobia. The affected vision as well as eye muscle disorders including strabismus, paralyses and contractions have been worked over rather thoroughly in the literature on the subject.

For some time the ophthalmologists have recognized a close relationship between intense emotions and acute glaucoma. They have accepted emotion as an exciting cause of glaucoma. Inman in citing his experiences states that, although consciously any emotion may not be present, the attack of glaucoma may coincide with the anniversary of events once "pregnant with emotion". He advocates a study of these cases for mechanisms and for treatment by way of providing a discharge of the emotions through legitimate paths. He has had several suggestive cases and advocates psychopathological studies of an organized nature, as direct questioning often fails to reveal anything of significance. He has often observed that acute glaucoma has a tendency to start on the anniversary of the death of intimate ones in the family.

Hysterical deafness as well as irritability to noises are often the outward expressions of inner difficulties. The irritability to noises is sometimes engendered from the annoyance the noise causes in preventing the patient's maintaining a mental concentration on his feelings and troubles. These patients are usually psychically depressed. Some complain of thumpings and buzzing in the ears which may really come from mild chronic catarrhal disorders and others spend much of their time listening to the arterial beating which any one with a little concentrated attention may learn to do, and those who do not understand the physiology of these parts seize upon the phenomena as foci for phobic organizations.

Anosmia is a disturbance in which the mechanisms are similar to those found in hysterical blindness. Some of these subjects are unable to smell perfumes or ordinary odors, but are able to detect more dangerous ones, for example, they may make their escape from a room which contains a small amount of gas which they interpret as being dangerous to their life or health.

There are also may phobias of personal significance connected with various odors which may or may not have a direct sexual or scatological implication. It has long been a well known fact that the closest relationships exist between the nasal apparatus and the sexual organs and functions, a connection which has philological as well as phylogenetic, developmental and pathologic aspects. Remarks on these relationships have been made by Aristotle, Celsus, Hippocrates, Tennyson, Shakespeare, and by William Lilly, the early astrologer, as well as in such sacred books as the Songs of Solomon and Ayurveda, the sacred Hindu classic of remote antiquity. Zola, Tolstoi and Lombroso also commented upon naso-sexual expressions in behavior, and moreover the laity are wont to refer to a "honeymoon catarrh".

McKenzie many years ago (1884) commented on the early history of this concept and W. D. Stimson (1929) made an interesting contribution to the subject from the viewpoint of the rhinologist, and many of the following remarks are taken from his paper. The ancient astrologers held that Venus presided over the nose as well as over all other parts pertaining to sexual organs. From a more scientific standpoint De la Chambre said that there was

no doubt of the relationship between the nose and the sexual organs.

Stimson emphasized that the erectile tissue in the nose (over the inferior turbinate, the dependent border and the posterior extremity of the middle turbinate and over the adjacent portions of the nasal septum particularly the tuberculum septi) is identical with that in the genitalia and referred to the case reported by Heschel in which hypoplastic genitalia were associated with absence of both olfactory lobes of the brain.

Orgasms in females have occurred from massage of the turbinates indicating that nasal stimulation may reflexly stimulate the sexual apparatus. Priapism has been found associated with retention and blockage of irritating substances in the nasal passages and cured by the proper treatment, but Stimson could find no instance of a case of priapism being voluntarily induced by nasal stimulation in males, but one man could bring on epistaxis by masturbation; this bleeding relieved headaches from which he suffered from time to time.

Schaeffer offered a neurologic explanation of these relationships. He pointed out that since the trigeminal nerve carrying afferent impulses from the nose establishes relationship with somatic and sympathetic efferent neurons of various motor cranial nerves and of the upper spinal nerves, it is highly probable that similar relationships are established with the dominant vasodilator center probably located in the medulla. The dominant vasodilator center is known to have a connection with the subordinate vasodilator center in the lumbar cord, thus establishing a complete circuit from the nasal cavity to the erectile tissue of the genital apparatus.

Fliess in 1897 stated: "In the nose the erectile bodies are under the control of the sphenopalatine ganglion, which receives sympathetic fibres from the carotid plexus through the petrosus profundus nerve. There would thus be an anatomical path to the sympathetic which controls the sexual functions as well." Apparently from a clinical standpoint the female more often than the male reveals these interrelations of functions, among which are engorgement of nasal cavernous tissue during the menstrual periods, causing epistaxis and headache; aggravation of sinusitis during menstruation and pregnancy (often associated with ovarian dysfunction); reflex pains over sinus areas in pelvic displacements and congestions; and "sympathetic engorgement of the erectile tissue of the nose similar to that occurring in the nipples of the mammary glands during sexual excitement and leading to sneezing, coughing, asthmatic attacks, rhinorrhea or simple nasal obstruction."

The total loss of taste is known as *ageusia*, a phenomenon which apart from definite organic disturbances is of comparatively rare occurrence. However it is sometimes seen in hysteria. Taste peculiarities and fault-finding with fo d, however, are very often a part of the behavior of the psychoneurotic whose idiosyncrasies may make him an exceedingly disagreeable guest, particularly in hotels where he feels privileged to complain about underdone, overdone, spoiled, or "rotten" foods.

A large number of skin conditions may be initiated, complicated, aggravated, or perpetuated by emotional factors. Blushing, blanching, localized edemas, sweating, goose pimples and elevation of the hairs are common familiar reactions to such emotions as shame, guilt, fear, anger and erotic urges. A very extensive literature deals with a wide variety of skin responses. Among these are examples of "stigmatization" due to autosuggestion under the influence of religious ecstasy first presented in the case of St. Francis of Assisi and recently brought sharply into focus in the study of Therese of Konnersreuth in Germany. Somewhat similar skin lesions are reported as experimental results in hypnotic investigations of susceptible individuals. As a matter of fact and of common experience many if not most persons feel itching sensations as the result of suggestion from the mere mention of itching or of crawling insects; or while observing another person scratch a part of the body.

The relationship between the emotions and the skin is not confined to the skin disorders as

such, but these disorders seem to affect people in a special way. They are inclined to overrate the seriousness of such conditions. One might assert that this is true of the disorders of all special senses. People become particularly uneasy when something happens in any one of these zones and perhaps for good reason, biologically speaking, as the sensory apparatus is the prime medium that keeps us in contact with our surroundings and it is and always has been the avenue of all of our experience.

As far as the skin is concerned, some of the unpleasantness may hark back to the era when a skin lesion, if extensive, frequently indicated a well known dangerous disease (syphilis). Social inheritance passes along many ideas from generation to generation. Moreover, the fear of contagion, the loathsomeness of the idea and the degree of disfigurement all play important parts. Premature baldness, patches of psoriasis and the pimple marked faces from acne vulgaris often create serious feelings of inferiority particularly in those unable to develop compensatory counteracting features. Pathological itching is a particularly difficult matter to fit into the pattern of social integration.

Esquirol was the first observer to attach a very particular significance to the word "hallucination", which he understood to mean that "a person labors under a hallucination or is visionary when he has a thorough conviction of the perception of a sensation when no external object suited to excite this sensation has impressed the senses"; Also, "I have proposed the word hallucination as having no determinate signification, and as adapted consequently to all the varieties of delirium which suppose the presence of an object, proper to excite one of the senses, although these objects may be beyond their reach."

Hallucinations were not regarded by Esquirol as caused in any instance as pathological conditions of the organs of sense but as strictly cerebral or mental in their origin. He said, "The senses are not concerned in their production; they occur although the senses do not perform their functions, and even though they do no longer exist." In this he obviously did not agree with Sauvages, who had given the name "hallucination" to errors resulting from a lesion of one of the sensory elements, nor with Dr. Foville, who had demonstrated lesions of the sensory nerves in patients who had been hallucinated. Among these early investigators it was emphasized that hallucinations might exist without insanity but they were found by Esquirol in 80 per cent of insane patients. Later Baillarger recognized the possible duplex origin of hallucinations, calling those "psychosensorial" originating in a combination of sense organ disturbance and "imagination" and psychical those due to a disordered mind without disease of the sense organs, or as Brierre de Boismont called them, physiological as distinguished from "pathological" or what now would be termed "psychopathological".

Similar ideas have been carried along with very little alteration to the present day psychiatry, but naturally there have been many modifications of the static "organic" concepts as well as of the attitude expressed by Montaigne in the statement: "It is probable that the credit of visions and enchantments and other supernatural influences, is for the most part to be ascribed to the power of the imagination over the unenlightened minds of the vulgar."

In order to demonstrate a clear cut psychosomatic situation which integrates a number of organic and toxic conditions and also more personal, complex and unconscious dissociations, I shall present some notes on a unique case of sensory disturbance, showing transitional stages of importance in psychopathology. The condition finally involved a number of the special senses.

A man, aged 72 years, with the appearance of being bright and alert mentally for his age, consulted me for a condition which he correctly considered to be a most unique situation. He was known as a very capable and brilliant man. He began to lose his eyesight, about 7 years before he came to see me. This loss of eye-

sight was accompanied by a series of very peculiar visual experiences.

He immediately began the description of his disorder, which had been gradually increasing from simple beginnings to hallucinations which in the patient's own words were "bizarre, grotesque and horribly disgusting things until Dante's Inferno would be a pleasure garden compared with what I saw every night." It should be stated here that the patient's condition started with cataracts forming on both eyes. He was operated on unsuccessfully and had been gradually afflicted with blindness until at the present time he could distinguish little else except light and darkness and the faint outlines of such objects as furniture and persons. If he would stand very close to an object he could get a fair idea of its outline, and by bringing his face almost close enough to touch the examiner he was able to determine that he was a "comparatively young man".

The hallucinatory experience began as follows. The first thing the patient noticed was that whenever he remained in a dark room or would turn out the lights to retire, the room would appear to remain illuminated and he could visualize various designs like wall paper patterns on the walls and ceiling. These patterns would change in an interesting manner. Then stripes and blocks and other patterns of various bright colors would appear. For quite a period of time these first experiences were characterized largely by changing color impressions, which later became complicated by a different picture. The next development was that in any darkened place, particularly in the night, he could see a sharply outlined circle of light, something very similar to the type of light that a circular lens of a projection lantern would throw. After watching this circle of light for a short time people and other objects would appear. Sometimes they were pleasant and at other times somewhat bizarre and annoying. Occasionally during this period he would see a man and a woman appear in this circle of light and kiss each other. This happened several times but he would admit of no other erotic or "sexual" visualizations. Soon after this and continuing to the time of the interview with increasingly bizarre motives, there appeared people and curious objects in his immediate vicinity. The circle of light no longer existed as the delimiting or focalizing element but the things began to appear everywhere.

Most of the characters were small and grotesque, the most outstanding thing being a red, open, mouth which he mentioned repeatedly. It would sometimes seem that a surgeon with several assistants and many others standing around would operate on various people, standing up very close to them and cutting huge pieces of flesh out of their faces, passing it on and feeding it raw to the bystanders. These bystanders, most of whom were bizarre gnome-like little creatures, would eat with peculiar motions of their mouths, with blood dripping down from their chins, together with a spurting out between the teeth of a sort of green-appearing fluid.

Often the patient had olfactory components as well at which times the meat seemed to be like carrion and gave off a terrible stench so that he would be nauseated to the extent of actually vomiting. Each night as these perceptions continued the actors would get closer to the patient and they became, as he said, uncomfortably near. At times he had seen this surgeon gouge out eyes and one subject he was working on had eyes covering the entire face, that is, there were numerous eyes looking in various directions. These remind one of the drawings of some schizophrenics. These eyes were gouged out and fed to the bystanders, being thrown into their red open mouths. This business went on night after night and was very disgusting to the patient. He claimed that his powers of description were not sufficient to tell all of the horrible things he saw. Sometimes this surgeon would rip off large sections of scalp with the hair attached, using a long knife with which he would then cut off the hair and feed it to his "assistants". The parties accompanying the surgeon were practically always referred to by the patient as "assistants".

The best description I could obtain of this hallucinated surgeon was that he seemed to be outstanding among the tormentors and was a medium-sized fairly slender man with gray hair and gray beard which partly covered a horrible appearing mouth.

At the time these notes were made the patient realized that this was going to persist throughout each night and he had the uncanny feeling that these people were getting ready for him long before he retired to bed. It seemed to him that long before he entered his bed room they were stacking up their assistants like blocks of wood around the wall and were all prepared to mobilize them for work by the time he was ready to put his light out. If he did not put the light out right away, they waited for him, as he could see them standing in the shadowy appearing corners of the room.

Another curious thing occurred during these "operations"; a spray was continually going in the room, a spray of fluid reminding one of the old Lord Lister method of disinfection in the early days of surgery but this fluid seemed to come from the mouths of snakes. At times he could feel it strike his face (here touch is involved) particularly on his closed eyelids. Therefore, he often prepared for sleep with a towel across his eyes. In other words, even though he had insight, as I shall stress later, he reacted to these experiences as though they were present in reality. He emphasized that there was no way to shut out these experiences; "If one should put 10 mattresses on top of the head one could see all the plainer because it would be darker. I can see them through my hand, although my hand is tightly covering the eyes, and they have a tendency to get closer and closer and I have often felt some of the small ones on my body." The thing which disgusted him most and caused nausea was the flesh eating. He felt that he did not sleep at all at night, but had to make up for this in the daytime to a certain extent. Sometimes these little people pulled long red inflated bags, appearing something like a sausage out from his skin. These, when broken, emitted a sticky fluid-like substance. "Not exactly a fluid, but I don't know what it is. Sometimes if I get up and swing my cane about I can drive them out of the room. Of course, the cane does not hurt them. It goes through thin air and I realize that they are not exactly there, but I have discovered that if I put a powerful will-force behind my actions, making believe after a fashion that they are really there, I can actually drive them out through physical effort, but lately I am beginning to wonder if there can be some basis in reality, for the other night when I hit some of them I heard a dull thud (auditory component) and felt a feeling against the cane of about 10 pounds resistance, so I am beginning to wonder if there is any materialization to this." It is possible that we have here the very beginnings of a delusion formation, at least the doubt has crept into the mind of the patient, engendered by his many nights of suffering.

The patient also saw at night many funny little brownies working about and these also appeared occasionally in the daytime. They are practically always accompanied by pleasant feelings. At these times he has also seen elephants, birds, cats, dogs, squirrels and foxes. Occasionally, particularly in the daytime, he visualized beautiful scenes of fields and meadows and flowers and birds in combinations. "They are something prettier than one could ever see in reality. I wish I could retain such scenes in memory. These scenes often occur in the afternoon when I am sitting on the porch." He was recently beginning to smell odd odors and to have physical sensations in connection with the more unpleasant visions and he was able to pull some of the beforementioned long, red inflated bags out of little pimples on the skin of his arms. While taking a bath one day he noticed some little bumps on his forearm. He picked at these and was able to pull out some of these bags. He had seen the surgeon in the night pull such bags from his subjects. These bags emitted the same type of fluid. After the bags came out there were open sore places on the arm which rapidly closed, soon becoming the size of a pinhead and then disappearing leaving natural

skin, but a peculiar sensation remained for a time. The patient was also able to pull from his own body various peculiar skeins of white flimsy material. His description of it reminded one of the accounts of ectoplasm offered by Spiritualists. He was almost, but not quite, able to hallucinate these things during the examination hours, but the room was too light to accomplish this successfully. He had also hallucinated sores on his own body.

He occasionally did not try to drive the grotesque scenes away, but in experimental moods let them have a free hand. They then got closer and closer until they were heaped all over his bed. Sometimes men of ghostly appearance with nasty, open mouths were over his bed and on top of him. He could even feel their weight. He endured these hideosities for a time, then drove them away. Sometimes they started out being only an inch or two long, gradually growing to 10 feet in length. In other words, they became Brobdingnagian in dimensions. He had also seen many little snakes which sometimes began by running about on 4 small feet and then turning into normal sized snakes. He disclaimed having any particular fear reactions toward these events, but emphasized only disgust. A few hours previous to one of our interviews he had noticed an additional feature. When his daughter-in-law told him that he could go to bed and that his bed was nice and clean (she at the time was escorting him into his room), he looked at the bed and saw some peculiar substance on the sheets and three men were lying there in the bed snoring. "Of course, the poor girl could not see these things—they are all in my imaginations." The patient seemed usually to have a full realization that these were purely imaginary experiences. He had never had any clear auditory hallucinations and these hallucinated men communicated with him only by gestures or menaces, though very little of the latter. As he expressed it, "They are more of an abusive nature." He then remarked: "You would have to have cataracts in order to see such things. I believe they are entirely dependent upon the local irritation of the cataracts and I know such things do not exist in reality, but I am always wondering why the cataracts should produce such things. I am losing my contacts lately and have nothing to live for except my tobacco. Sometimes my relatives read to me, but they don't do it enough and it is the only contact I get with my surroundings, now that I am so nearly blind. Whenever I talk to people, particularly to physicians like you, who are interested in these things, I feel better. I think they are made worse because I have nothing else in the world to make contact with. I am sure the physical events in connection with them are imaginary, but I can't seem to correct these experiences in a way that will stop them. It sounds like a lot of crazy talk, but I do not think that my mind is fundamentally affected, but the cataract is at the bottom of it all."

The last development in his case as far as the hallucinations were concerned, was another type of experience in the form of women who would approach his bed, holding their hands out toward him and would stroke him on each side of the face and under the chin with the palms of their hands. These were not interpreted by the patient as erotic in nature, but they were mysterious, peculiar gestures. He also stated since his wife died that he had once hallucinated her lying in his bed. Recently during his meals he was able to see a flimsy peculiar material covering the food, which disgusted and nauseated him to the extent that it was seriously interfering with his nutrition. Also the impression of actual physical contact with these men with the wide open mouths was becoming more and more prominent and he recently awakened from a sleep, finding several of them sucking with "these nasty mouths" on his legs below the knees. It was a disagreeable sensation, but not painful, although it persisted for some time after he was awake and after he had driven away the hallucinated objects after the fashion before mentioned in the account. These last experiences were crystallizing very definitely into delusional ideas as he was gradually losing

his ability to correct the impressions in terms of the actual situation. He finally decided "they must be real".

Visual hallucinations in sane people with various lesions of the eyes are not uncommon events, but I have been unable to find in the literature any case having hallucinations of such complexity and of such a wide variety of implications as in the case cited. Ormond, the ophthalmic surgeon at Guy's Hospital, described cases of visual hallucinations associated with eye conditions. These patients were annoyed by grotesque faces which were usually at first amusing, but later became disgusting, revolting or annoying. He also related a note from the old book (1854) on eye disorders by MacKenzie, wherein the patient Nicolai Berlin, book seller, had hallucinations of this nature and had recourse to leeches, which gradually resolved the hallucinations. Macnamara pointed out that cutaneous and visual hallucinations are associated in these cases. He reported five cases of cutaneous hallucinations in patients who retained normal affects, were properly oriented, showed good powers of judgment and no mental disease apart from their hallucinations. One of his cases had many experiences similar to my patient, that is, black things, and materials resembling cotton, filth and debris came out of the skin. Occasionally this man had respiratory difficulties and complained of suffocating feelings, after which bits of thread seemed to come out. It is quite interesting that in these cases of sane people with hallucinations they are often very reluctant to tell the family physician or surgeon for fear that the reaction will be interpreted as psychotic in nature. They are, therefore, apt to relate their troubles in a very confidential manner and only after the physician is sworn to secrecy.

Regarding the hallucinations of diminutive human beings, it should be emphasized that they have been frequently mentioned in the general literature under the term "Lilliputian experiences" as borrowed from Swift's account of Gulliver's Voyage, but in the medical literature microptic hallucinations have been seldom mentioned. However, accounts of the affective states accompanying these experiences by Leroy, their appearance in a hysterical convict, as related by Yanger, in hyoscine poisoning by Vonderahe and other accounts by Conklin and by Alexander should be mentioned in this connection. Leroy describes these visual hallucinations as occurring in hypnogogic states, narcoses, cerebral arteriosclerosis, skull injuries, in toxic and febrile states and associated with epilepsy as a form of aura. In such hallucinations the subject sees small visions, usually human in contour, phantastically costumed and engaged in all sorts of activities. The actual objects seen in reality by the subject appear to be normal in size, shadowy and colored, thus differentiating this state from conditions of complete micropsia, in which the objective stimuli are all perceived on a small scale. It is said of this type of hallucinations that their emotional content is almost always agreeable, which, as we may remark, was usually the opposite in the case of my patient. The affective state of the patient undoubtedly determines the emotional situation in which the hallucinations take part. Leroy considers such hallucinations of great importance, as they seem to show clearly a relationship between cortical centers and activities of the psyche. The cortex, he regards as being stimulated by a toxin, which at the same time depresses consciousness, that is, normal consciousness is depressed, but the cortical centers are irritated. The pleasant emotional character of the hallucinations may be accounted for in part on the basis that the visions themselves are simple and harmless, but particularly because the subject unconsciously believes, or has believed once in his childhood, in a world peopled by small beings who occupied themselves with agreeable pastimes. This principle, which attempts to explain the agreeable emotional tone, may hold true also in contrasting instances in which such hallucinations are concerned with small demons and horrible activities, invoking terror of the same type which the subject believed in

during his early life. Flournoy has reported a case in which Lilliputian hallucinations began in a man of 86 who developed cataracts and coincidentally with considerable diminution of his sight. This man also had some elementary illusions, luminated images, as well as the hallucinated small objects.

The toxic element is probably in active force in many of these reported cases and perhaps played a part in my own patient, as at times he was receiving fairly full doses of morphine in order that he could get some sleep at night. Undoubtedly the local eye irritation in some of the cases reported is the releasing factor in the causation of hallucinations in that the patients are not fundamentally psychotic. However, mechanism and content are two different matters. The interpretation of the content of the hallucinations should be taken into consideration.

According to Freud, in the process of recollection the mind tends to follow a regressive path and to allow the memory traces of past experiences to again appear in consciousness in the form of visual shapes, while the process of search for the desired experience is going on. The dream work utilizes this train in its transformation of latent thoughts into the perceptual forms. This repetition of thought by visual images has been included in the term regression and it has been emphasized that during the day this process may be voluntary, but sometimes involuntary, as in the case of the hallucination. The mind follows a regressive path and produces hallucinations as well as dreams.

We will be able to understand the personal basis and determinants of these particularly sadistic hallucinations I have described if we know the following facts regarding my patient's occupation and something about certain experiences in early life. The description of the hallucinated surgeon according to the patient's son fitted perfectly the appearance of his father, that is the patient himself, several years ago when he was engaged in surgery as a profession. He had studied medicine, became a general practitioner, and then entered the Navy where he became a surgeon, being at one time an expert amputator, holding the record for speed in double amputations of the legs, which fact gives one a lead toward an understanding of the "operating" room analogies in most of his hallucinated experiences. He most certainly did not recognize himself as the "surgeon". The patient himself, in referring to his childhood, said that he thought that something of an explanation might be there, or at least certain early experiences might be of importance. He then described what he alleged was called "blind staggers" in the country where he was reared: a sort of disorder that is usually ascribed to horses suffering from attacks of confusion, but a condition which he had heard described only on two early occasions. During the period of time starting as far back as he could remember up through his childhood, he recalled that on certain occasions, particularly when he would look at a bright object when the sun was shining or when he was suddenly confronted with an unusually dazzling bright object, he would begin at first to feel a slight dizziness, then a tingling sensation in one foot, which would gradually creep up over his entire body, including that side of his head and the appropriate half of his trunk. This feeling would go on to complete numbness, although not quite to paralysis and sometimes would be followed by vomiting. He would occasionally induce vomiting in order to feel the relief afforded. He would not become unconscious during these attacks, but said that his memory would be disturbed for a short period for the names of neighbors and for some of the small objects in his environment. These attacks would last for 25 minutes or so and then were followed by terrific headache, usually on the same side of the head and occasionally covering the entire head. These would last with decreasing intensity for about 3 days. He remembered several such attacks. It is of interest for us to speculate whether these were migrainous in character, were epileptoid equivalents or were hysteroid expressions of traumatic or other primary signs, but as the patient was growing

worse very rapidly and was becoming more confused and delusional mentally, it was recommended that an operation be performed. This was done and the patient recovered completely mentally. His hallucinations vanished with the regaining of his eyesight, which while not complete, was restored to a remarkable degree.

While a complete study of this multifaceted condition was not possible, enough was accomplished to indicate the nature of typical psychosomatic problems and to show glimpses of the interaction of the predisposition, the personality, the exciting cause, the symptom formation, and the evolution of a special type of delusional formation.

I should now like to present what I have here termed the *peripheral hyperalgesic neurosis* by beginning with some generalizations about sensibility, then passing to particularizations regarding its disturbances in a certain type of case, and finally comment upon some possible etiological explanations or leads.

It has long been recognized that general sensibility is altered by the emotional state of the individual. History has furnished many classic examples, we have all witnessed, and many of us personally experience states of intense and prolonged emotion, in the absence of mental representations of pain during which the general sensibility may be more or less completely deadened. Such conditions may occur under the effect of either sthenic or depressive emotions. Soldiers in the midst of battle, people in fighting fire or in the turmoil of accidents, or participants in the interpersonal exchange of fisticuffs, may be seriously injured without recognizing the fact until it is pointed out by another or until the emotional tension has been reduced. A mystic elevation of the mind or religious emotion may engender the same effect as the history of the persecutions of various saints and martyrs ably testifies. The pain disjunctions seen in hysteria and in certain cases of schizophrenia are too well known in clinical psychiatry to justify more than this passing comment.

On the other hand when people are expecting something to be painful, the phenomena of sensibility receive a psychic reinforcement, and many individuals have an impression of the pain before the expected painful stimulus has touched them. In the case of the patient who screams before being touched, the cry is sometimes brought forth by fear, but it is also often true that there has been a realistic mental representation of the pain which the patient is even able to distinctly localize. Moreover, under such conditions, actual pain is reinforced to the extent that a simple touch becomes extremely painful, which would scarcely be perceived without the emotional expectancy of pain.

Such experiences must prepare us to believe that hyperaesthesias are frequently phenomena of suggestion, due to a psychic fixation on one or more parts of the body.

The so-called "phantom limb" is a sensory experience or hallucination that has been studied rather extensively, as it has features of interest to the neurologist, the psychiatrist and the surgeon. It usually follows the sudden loss of an extremity by amputation, and seems to be very rare in cases of congenital amputations or amputation by slow degeneration of tissue or loss of limbs by freezing. In some cases the experience of repossessing the absent limb is merely annoying while in others there is algohallucinosis of severe pain often persistent and demanding radical interference.

Nearly all persons having had a sudden amputation suffer from some phantom sensations, but only about 6% (Pool) suffer from pain. The burning type of pain resembles the causalgia of Weir Mitchell. In another type the limb seems to be in a cramped painful position. Some etiological concepts concerning the disorder are based on peripheral irritation of the nerve stumps or on scarring, others are involved in neuromatous growths, while still others consider that the concomitant psychological aspects are of equal or greater importance. Some of the painful situations are exceedingly difficult to relieve. Resection of neuromas, infiltration of the sympathetic chain, sympathectomy, posterior chordotomy

(Pool) and even resection of the parietal lobe of the brain have relieved many patients and have also failed in other cases. In a case of reactive depression and phantom pains following amputation, electric shock therapy has removed both the pain and depression (Pisetsky).

One interesting phenomenon emphasizing the complexities of this type of psychosomatic problem is seen at times involving the body image. The patient awakens from sleep, feels the presence of the amputated member; then as he becomes reminded of the true situation the hallucinated limb gradually becomes smaller and smaller attaining the dimensions of an infant limb before it disappears altogether. Thus it appears that this part of the body image that has been destroyed regresses in the hallucination over the same path by which it was constructed progressively over the years of bodily development and awareness. The pattern of regression thus seems to hold here as it does for behavior at other levels of integration, and the whole question is in need of elucidation by further research.

It has long been known that a continued emotionalism may create a state which if not that of hyperaesthesia, is at least one of hyperexcitability, in which all contacts are painful and result in sharp reactions, a state of hyperexcitability which in most cases distinctly produces an exaggeration of the reflexes. These disturbances of sensibility are not, of course, confined to the skin alone; mucous membranes, muscles and bones are subject to them, so what has been said about emotional reactions may be applied to all points of the body on which any traumatic action is liable to cause a mental representative of pain.

The expectation of pain would at first appear to be a result of reason. In some respects this is so, but expectation alone is not sufficient to create phenomena of psychic reinforcement of pain. When expectation is reflective and analytical or "cold", popularly speaking, it does not increase pain, but may even decrease it, a phobic element is necessary, but what we desire most is to learn what is behind the phobic element. We know also that emotion engenders and in some organic cases enhances sensations of thoracic tension, impressions of painful contractions in the abdomen, painful genital and perigenital sensations, and in neurasthenics a horde of algias which have no other known origin.

The disturbances of sensibility as encountered in the psychoneuroses are of two kinds, i.e., purely subjective disturbances and those which lend themselves to objective study, the latter being of two varieties, the phenomena of anesthesia and of hyperaesthesia, and which are usually a part of hysterical dissociations, and conversions. But here I should like to present some particulars regarding a syndrome of subjective disturbance of sensibility in which there is practically nothing of an objective nature gained in the neurological examination, and regarding which there is nothing of a detailed nature in the literature of the psychoneuroses.

In the course of my experience in neuropsychiatry I have found but few of these patients. They are not neurasthenic as you will note, as the description proceeds. I shall outline the presenting symptoms in the last three cases examined, not in the usual detail of positive and negative findings in such cases, which is too often tedious to listeners, but rather as to similarities and dissimilarities between them. They came from three occupational levels or walks of life.

One patient was a 50 year old laborer whose work was to fit heavy steam pipes, chiefly in out of door places and in damp cellars. There was considerable heavy lifting connected with this work. His chief complaint was hypersensitiveness of the skin of the legs as high as the knees and a "grinding-aching" of these extremities with some tenderness along the sciatic distribution. There had also been pains in the forearms. At first these pains had been present only occasionally to the extent that he would have to rest a day at home, but recently they had become more or less continuous for two months during which he had not been able to work, and was supported

by his son, a grown man with a family of his own. He had consulted two physicians, both of whom had made the diagnosis of muscular rheumatism.

Another patient was a 52 year old architect and designer, who had made himself at least locally famous for his excellent work. At the time he was referred to me for consultation he had done very little work for over a year, and finally could not drive his own car. During this time he had consulted dozens of doctors—some of them neurologists—and had taken all of the known medicines and other forms of treatment for neuritis, neuralgia, and muscular rheumatism. He was a very breezy, ingratiating, extraverted appearing fellow at the time I saw him, so eager to discuss his symptoms that he began to describe his pains before he could remove his overcoat. He described tingling sensations in his hands and steady boring pains in the fingers and wrists, at times reaching as high as the elbows—to a lesser extent he described similar pains in the feet and legs. Perhaps from suggestions received during former examinations he thought there had been some atrophy of the interossei muscles and he had a curious way of holding his thumb to produce the appearance of a cavity in the first dorsal interosseous muscle. Although there were always some disagreeable sensations and soreness to the touch present in these areas, the chief complaint was of paroxysmal attacks of severe aching, during which he had recourse to luminal internally and bathing of the affected parts in "rubbing alcohol". Frequently during these attacks which lasted until the sedative took effect, he also suffered from a band-like sensation about the head and some dizziness.

The third patient was a 55 year old lady of culture, fortune and leisure, a spinster who had spent most of her life in travel, leading in a way a very active existence. I was called to one of our local hotels to see her. She was in the midst of one of her attacks and was surrounded by physicians, one of whom had called me for an opinion, as he was under the impression that the patient was threatened with cerebral hemorrhage. She had an anxious facial expression, was perspiring freely, was uneasy in the bed, opening and closing the hands, rubbing the forearms, and complaining bitterly of peculiar "grinding" sensations and extreme pain in all four extremities. Upon examination I could find no differences on the two sides of the body, nor could I find any objective signs other than general intermittent hypertension of the muscles of all four extremities, and a rapid pulse. Fairly convinced that this was a severe anxiety attack in the presence of the patient I told the others that I was certain as to the nature of the condition and that I had a remedy in the form of a tablet that would stop the attack in just 15 minutes. The nurse administered the tablet while I was in the next room explaining the nature of said tablet, which was composed of sodium bicarbonate and magnesium oxide, and elaborating upon the immediate value of placebo in such conditions. The patient felt easier in 10 minutes, and in 15 the pain was gone, she was very tired and wanted to sleep; to the nurse she expressed her satisfaction that a drug had been found at last to stop such terrible suffering so quickly and efficiently. In order to study her case I made subsequent visits during which it was brought out that she had suffered from these painful paroxysms for six or eight years, the attacks always starting with "grinding", "trembly" sensations rapidly becoming painful, and accompanied by some anxiety, and lasting for a few hours, usually during the forenoon or a part of the afternoon. This last attack had been an unusually hard one.

To summarize some of the clinical facts characteristic of all these cases, one can state that:

1. Exhaustive laboratory examinations failed to reveal any leads worth considering.

2. General physical examinations were negative with the exception that the architect had lost some weight over the period of a year during which he was incapacitated. There were no signs of vascular involvements.

3. Neurological examinations failed to show

any sensory motor changes, or any objective disorder in muscular coordination and tone. In other patients with hyperalgesic components in their neurosis I have sometimes found an uneven or intermittent hypersensitivity to cutaneous irritation, for instance, a pin prick is felt to be really painful, a warm bath is felt as extremely hot to the affected parts, and pressure on the deeper tissues, fat tissue or on the groups of muscles, causes great pain. In my present three cases the complaints of spontaneous pain and hypersensitivity were very strikingly out of proportion to the reaction given to actual pressure and manipulations of the parts usually made in a neurological examination.

4. In some patients with neurotic hyperalgesic symptoms, Valleix's points, the points douloureux, those tender points in the course of certain nerves having some diagnostic significance in the neuralgias are much more sensitive than in normal persons, but this was not a characteristic of my three patients under consideration: also the painfulness of the great nerve trunks may resemble that of neuritis, particularly the symptom of bilateral or unilateral sciatica, and sometimes the brachial plexus seems to be involved. Of the three patients the laborer had occasionally subjective symptoms resembling those seen in sciatica, but these were not pronounced.

5. All three had the pains alternately in the muscle groups of the extremities, which painful sensations tended to develop fairly rapidly, and change rather suddenly from complete well being to an attack, and then disappear shortly, or again persist for longer periods. Even during the more acute attacks deep pressure on the muscles was not as painful as one would expect from the verbal complaints of the patients.

6. Another interesting point is that the complaints of these patients greatly resemble the symptoms of so-called muscular rheumatism, thus probably often leading to a mistaken diagnosis, and again obese patients with the disorder may lead an inexperienced diagnostician to the impression that he is dealing with some type or degree of adiposis dolorosa, fibrositis or panniculitis.

7. Although one sometimes finds in these cases some of the clinical signs of neurasthenia, such as tremors, exaggerated reflexes, fluttering of eyelids, excessive lability of the nervous system, etc., it is my impression that relatively very few give the general impression that they are the so-called neurotic persons in their every day life. Certainly my three patients did not show these traits to any remarkable degree.

8. Hypersensitivity of the scalp I have noted in some cases, which is usually accompanied by annoying headaches, but in the present group the architect, only, complained of this symptom.

Thus, taking the whole situation into consideration we are confronted with either an obscure organic disease in the strict sense of the word, or with some curious so-called psychic fixation of an impression of pain. The question now comes automatically—What is the possible etiology? In the famous words of Claude Bernard "I shall confess my ignorance at once and then proceed."

1. As has been before stated, no leads were obtained from the orthodox laboratory examinations, which of course is not to affirm that no clinical changes were present in the bodies of these patients, and particularly in their muscles. It is possible in such states that the muscle components are affected; the glycogen, adenylic acid, inosinic acid and hypoxanthine bio-activities are as yet not well understood in this setting. The presence of oxalic acid in muscles, discovered by Stendel, brings up problems in muscle metabolism. So we must pass on to other fields at present.

2. As these patients in age are within the conventional involutional period (40 to 60 years), the question of the influence of distorted hormonal factors arises. This question of how much climacteric changes are responsible for the development of these disorders is preceded by the more fundamental question as to whether there is a climacterium in men. Most of those present will be pleased to know that it is answered in the negative by Jacobi, who accomplished a large amount of research on the

subject. He concludes that there is no sharply outlined climacteric period in men as in women. This author agrees with Hoche in the opinion that the climacterium in men is really represented by a very gradual, at times almost imperceptible change, which later blends with the involution and senile changes of the rest of the body. Consequently the influence, if any, is indefinite.

3. The work of Specht, Kuppers, and Hess in investigating the vegetative nervous system has done much to reveal its relationship to psychic processes, and also to the sensori-motor nervous system, where principles of reciprocal and coordinated functions are adduced. Hess conceives that the sensori-motor principle comes into being phylogenetically at the appearance of the metazoa or when the cells combine to form a commonwealth of cells. In the lower animals little light has been thrown on the relationship of these two systems, but it has been supposed that they stand in closer cooperation than in the more highly differentiated organisms. The preservation of the life of the cell, regarded as the aim of the vegetative nervous system, is in harmony with the preservation of the total organism, which is the main function of the sensori-motor system; however, in the control and direction of the circulation of the blood the two systems exhibit antagonism. In strenuous exertion of the total organism the sensori-motor system dominates the vegetative, while in fatigue the reverse is true. This reciprocal antagonism and interdependence is illustrated in the regulation of the heart's action, which, however, never yields exclusively to either inhibiting or stimulating influences, but tends to reach a condition of equilibrium between the two antagonists. Within the vegetative nervous system itself there is the same reciprocal antagonism between the two divisions, the sympathetic and parasympathetic, the former performing a role analogous to that of the sensori-motor system in regard to the total organism and even appearing as a connecting link between the sensori-motor and vegetative functions. On the other hand, the parasympathetic nervous system produces a diminished efficiency in the sensori-motor apparatus. A disturbance in the emotions influences the vegetative nervous system, giving it some temporary predominance, and Glazer's theory of the origin of psychic pain, being due to the changes in caliber of the vessel walls through the action of the vegetative fibres is an intriguing one in connection with these cases. Another element is important, and that is the education of the sensibilities as the result of attention to physical fixation points. There is no question but that one may succeed, by focusing the attention upon a part of the body, in educating a visceral or peripheral sensibility to hyperactivity, even to the point of suffering miserably from sensations of pain or fatigue, perhaps resulting in part from the increased tonicity of the parts. In one of my earlier cases a pending insurance claim helped this matter along considerably.

Certainly it is this type of neurotic behavior which I have mentioned as characteristic of my cases that renders differential diagnosis in the various rheumatic disorders difficult, and emphasizes that a so-called neurotic constitution may show painful myalgias and neuralgias —some of them could be called "pseudo-rheumatics", and many with hyperalgesic neurosis under the diagnosis of muscular rheumatism, rheumatic neuralgia or neuritis are subjected to various therapeutic measures without the neurosis being recognized.

Psychodynamics has maintained that the neurosis represents the working out of unconscious conflicts, and when organs or groups of organs are involved they may be in some way under the control of unconscious emotional factors. The aim of psychoanalysis regardless of whether it is applied to the group behavior or to the individual is to discover the *latent wish fulfillment formula* in each specific type of mental organization, just as it can reduce a dream or an emotional experience to such a patent formula. It regards the ego as split off from the same root as the id; the ego, however, develops under the influence of the environment —the id never leaves the phylogenetic cave.

We lead a double existence, that of a real man and that of a hidden being. As psychodynamics is still a new science, or at least the beginnings of one, it is highly probable that much time and research will be required to discover all the fundamentals of the integrated organism, but that should not prevent us from utilizing all of the tools with which we may work.

For external reasons my patients with this special form of neurosis were not investigated by the psychoanalytic method, but they were studied by the "fine toothed comb" method of history taking, and the historical findings were such as to justify one in taking certain liberties to speculate on the psychic etiology, basing these inferences in part on the indicators found by many investigators in hundreds of cases of neurosis studied by the analytic method.

1. All three of these patients were the active, doing, muscular libidinous types—what the Germans call the Manuale types of people—interested in moving about, and doing something, and particularly in overcoming obstacles. In these types the "Manuale territory", as it is called, gets its greatest development during the second and third years of life. The trend is active in character and when pathologically expressive carries a strong destructive tendency or sadistic component, the muscles being the chief organs of expression.

2. In addition to this trend, these patients showed an active hatred for the father, they were never able to get along with this parent, but were in a definite rebellion against him. There was evidently a need for self-punishment for the guilt these hatreds engendered, which also came out in connection with all authority, and there was an excessive reverence after the father's death, to the point of worshipping his memory. The feelings of guilt and the desire for self punishment certainly aggravated the symptoms if one does not care to place them in the principal etiological role. That an exaggerated feeling of guilt is the unconscious recognition of the ethical impropriety of an oedipus situation is a piece of constructural psychology which of course was not investigated in these cases, but there was no doubt of the feeling of guilt, and the crippling of the functions consciously most utilizable and desirable in the hyperalgesic type of person.

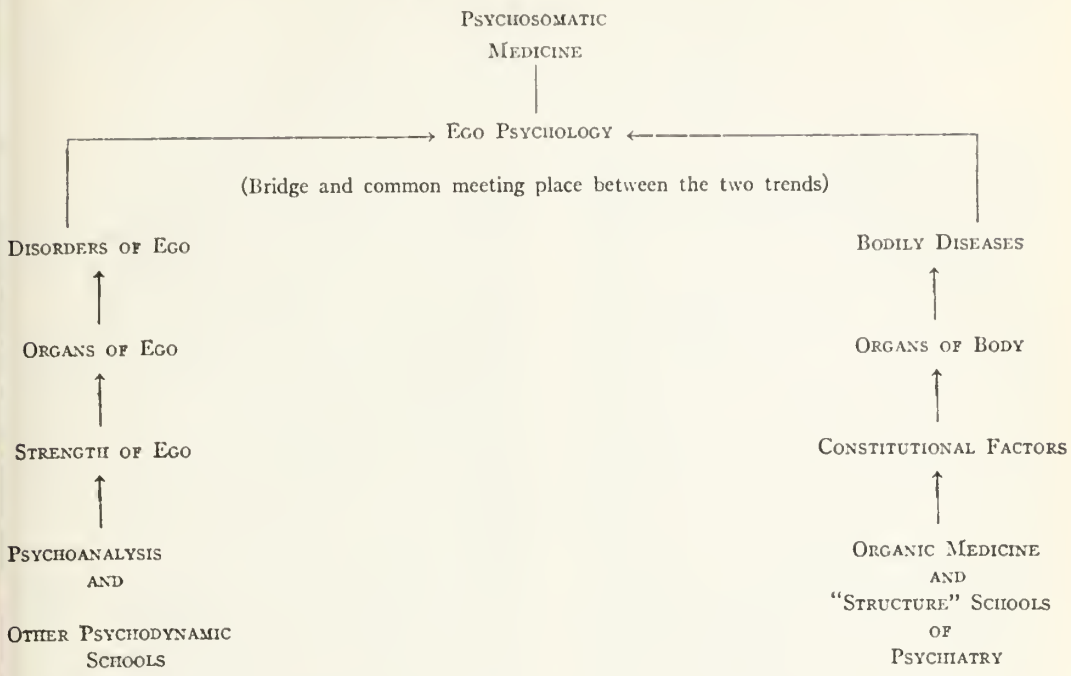
Every psychiatrist is aware of the fact that whenever he fails to detect the presence of an organic disease in a psychoneurotic person or in the "chronic complainer" this oversight is wont to bring accusations and criticisms of him in particular and of psychiatry in general. Our colleagues in medicine and surgery failing to recognize the true state of affairs in neurotic situations do not suffer the same condemnations for misplaced therapy. These difficulties and attitudes will be corrected in time, although probably mistakes in diagnosis will always be made occasionally if for no other reason than disease does not always manifest itself in accordance with the established rules and expectations.

When new criteria are observed or are suggested new light is cast upon a subject and a better understanding achieved. Unfortunately in these matters our knowledge is as yet at so low a level that all we can do is to follow along the lines of greatest probability and work with what we have at hand.

According to the second law of thermodynamics, the inorganic world tends toward disorganization. This differs from the distinguishing character of the biological world which is the tendency to build up, to integrate and to continue in organization and evolution. In biological investigation one may have a mechanistic approach or rather a dynamic approach without attempting to reduce the formulations all the way down to the level of already known physics and chemistry, as these at present probably do not explain the processes—a different or new physics and chemistry may be needed. In the meantime no air of mystery need be maintained concerning the psyche, evolution, heredity, regeneration, degeneration or other complex phenomena that present themselves for our interest and elucidation.

The psychoanalytic and other psychodynamic "schools" and trends are progressively going in for more and more what they term "ego psychology" and are giving an increasing

SCHEME OF RELATIONSHIP



amount of attention to disorders of the ego. They speak much of the "strength of the ego". At the same time the more "organic" structurally oriented "biologic schools" of general medicine and psychiatry, that is, those interested in the organs of ego, are turning toward and accepting so-called "psychosomatic medicine" which actually is the bridge between the two attitudes and the common meeting place. When analyzed down to fundamentals, ego psychology, the pet of the analysts, and psychosomatic medicine, the new interest of the internists, are one and the same thing. Practically the only difference is one concerned with semantics.

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Studies on Epidemic Hepatitis and Its Sequelae*

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THE Mütter Lectures of this College usually deal with subjects in pathology which are of interest to the surgeon. At first glance the title of to-night's presentation hardly comes under that designation, for epidemic hepatitis is customarily regarded as a "medical" disease. But hepatitis has important surgical relations, and may present puzzling surgical problems. Not infrequently the disease begins abruptly with manifestations that suggest an "acute surgical abdomen". Occasionally it may be ushered in by cerebral symptoms of such gravity that exploratory craniotomy has been performed. By contrast, the disease may develop insidiously, and pursue a protracted course with a deep and almost symptomless jaundice reminiscent of an extra-hepatic biliary obstruction. To a surgical technic, biopsy of the liver, we owe precise information of the hepatic lesions that occur in the most common, that is to say, non-fatal form of hepatitis. It is primarily the surgeon who is concerned with the problem of the hepato-renal syndrome. And, finally, it should be recalled that surgeons have played a significant part in clarifying the interrelation between dietary factors and liver injury, a linkage germain to the subject of our discussion.

I shall attempt to summarize present day knowledge of the nature of epidemic hepatitis, with particular emphasis on its pathology. The material which forms the basis of this study consists of over 300 fatal cases, mainly among military personnel; a somewhat smaller series of non-fatal cases studied by means of biopsies; and a third group in which the liver was examined after clinical recovery either by biopsy or postmortem.

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Historical Considerations

Epidemic hepatitis is not a new disease. It is endemic throughout the world; it occurs in all races and in persons of all ages, but it is most common in children and young adults. Epidemics may develop whenever and wherever large numbers of susceptible individuals are brought into close contact. In peace time relatively small outbreaks have been common among school children, in institutions and in camps. During times of war large scale epidemics have often affected members of the armed forces. In the last war the disease became pandemic. In the armies of several of the warring nations the incidence of the disease was at times so high as to constitute a serious military problem. For example Hatfield and Garrod state that the incidence among troops in the North African desert just before the battle of El Alamein reached 10 per cent; and in discussing the occurrence of hepatitis in the German Army, Dietrich in 1942, wrote that it had become one of the most important epidemic diseases. Large epidemics, however, are not peculiar to armies or to wartimes; Sweden experienced an outbreak in 1927 which is one of the most extensive on record, and at present the disease is widely spread in several of the Scandinavian countries.

Hepatitis has long been familiar as "catarrhal jaundice", a term reflecting the views of Virchow concerning its pathogenesis. He believed that the disease is caused by an inflammatory obstruction at the orifice of the common bile duct. This hypothesis received almost universal credence, and although it was never substantiated it influenced medical thought and practice for over half a century. The explanation why the essential nature of this disease remained unknown for so long a period is, in retrospect, not difficult. The course of catarrhal jaundice, whether sporadic

or epidemic, is nearly always benign. The mortality is low unless certain potentially injurious factors coexist; the rates in various epidemics have ranged from 0.13 to 0.44 per cent. Even these low figures are in all probability higher than the actual mortality, for commonly the disease may run an almost symptomless anicteric subclinical course. Because of the low death rate opportunities for postmortem studies have been comparatively rare. When, as during extensive epidemics, a number of fatal cases were examined the liver invariably has shown the changes of so-called idiopathic acute yellow atrophy of the liver—a condition formerly regarded as an entity unrelated to catarrhal jaundice. (Parenthetically, it should be pointed out that the term "acute yellow atrophy", coined over 100 years ago by Rokitansky, must be regarded as a misnomer which has no place in modern medical nomenclature. Originally applied to the hepatic necrosis resulting from phosphorus poisoning, it came to be applied to any kind of massive necrosis of the liver whether "idiopathic" or of known etiology.) In the late nineteenth century, the Danish physician, Flindt, brought together considerable clinical and epidemiological evidence linking these two conditions; unfortunately his work was over-looked. In 1912 the English Clinician, Cockayne, without knowledge of Flindt's work, again reviewed the evidence for relating catarrhal jaundice with idiopathic yellow atrophy of the liver. He came to the conclusion that both are usually due to the same cause, a specific organism of unknown nature. Since the first World War, with its many epidemics, a number of observers have stressed the parallelism between the incidence of catarrhal jaundice, and the frequency at the autopsy table of idiopathic acute yellow atrophy. Thus it became more and more a probability that benign catarrhal jaundice and yellow atrophy are but two extremes of one and the same disease. As a corollary the view gained ground that the site of the essential lesion of catarrhal jaundice is not in the extra-hepatic bile-ducts but in the liver. Moreover the nature of this disease came to be regarded—on evidence which at that time was slender indeed, but proved to be correct—as an inflammatory process, i.e. as a form of hepatitis.

Until the first World War there was no precise information as to the lesions of "catarrhal jaundice". During the war, Eppinger, one of the foremost students of liver disease, performed autopsies on three soldiers who during a typical though mild attack died of trauma. In all three he found lesions in the liver which he regarded as a "miniature form of acute yellow atrophy". Up to the outbreak of the second World War only a few other postmortem and two or three biopsy examinations had been recorded: in all, more or less central-zonal destruction of hepatic cells was found. The increased frequence of hepatitis, its prevalence in armies and its military importance during World War II led to intensive investigations which have finally revealed the cardinal lesions of hepatitis.

The term "epidemic hepatitis" was first applied in 1918 by Lindstedt, in contradistinction to "infectious hepatitis" or Weil's disease (leptospirosis), then erroneously believed to bring about extensive hepatic damage. Unfortunately there has been no uniform usage of the various terms employed. Recent advances in etiology suggest that this confusion may be resolved by the general adoption of a new term for this old disease, namely "virus hepatitis".

Etiology and Epidemiology

The causal agent of hepatitis has the attributes of a filterable virus. The virus has not as yet been cultivated, nor has an animal susceptible to it been found, although many species, including the higher apes, have been tested. At present the only means of demonstrating the virus is by transmission to human beings. In the past few years this has been accomplished with volunteers. Some of the most significant studies have been pursued by several of our colleagues in Philadelphia: Doctors Stokes, Neefe, and Havens. The virus has been shown to exist in the blood, the

feces, the urine and nasal washings. Under *natural* conditions it is usually transmitted through the gastro-intestinal tract by ingestion of contaminated food or water. Under *artificial* conditions the disease may be spread by parenteral injections of whole blood, plasma or serum from a person harboring the virus. Thus two main epidemiologic variants of virus hepatitis may be recognized; naturally occurring hepatitis (in endemic or epidemic forms), and inoculation hepatitis. The latter may develop after transfusions of blood or its derivatives (homologous serum hepatitis), after inoculation of vaccine containing small amounts of infectious serum (post-vaccinial hepatitis), and after injection of therapeutic agents through needles or syringes contaminated with blood from an infected person (hepatitis after insulin injections, certain cases of post-arsphenamine hepatitis, etc.). It is believed that the specific causal agents of these variants are closely related, but antigenic differences have been demonstrated. There is one outstanding clinical difference in the two forms: the incubation period of spontaneously occurring hepatitis ranges from 20 to 40 days, that of the inoculation type from 2 to 4 months. It is possible that this difference may be due to the mode of entry of the virus, or be a characteristic of the strain.

I wish to emphasize that, in agreement with the great majority of other students of hepatitis, I have found that in their clinical, biochemical and pathological manifestations the "natural" and "artificial" variants of the disease are entirely alike and indistinguishable.

Clinical Picture of Hepatitis

The course of hepatitis throughout many local or widespread outbreaks and at various periods of time has been remarkably uniform, although the symptoms and signs have varied in degree. A Philadelphian, Dr. Woodward, has given an excellent account of the clinical course as observed in federal soldiers during the War between the States.

"When this form of jaundice attacks a regiment or an Army, it usually appears in a number of cases simultaneously or in close succession like other epidemic disorders, lasts in each case from one to six weeks, or even longer, and then slowly disappears. The appearance of the icteroid hue is, as a rule, preceded by more or less derangement of the general health; sometimes, however, only by a few days of headache, constipation and malaise, and occasionally the discoloration of conjunctiva and skin is the first noticeable symptom. The color of the skin may vary from a scarcely noticable tinge to a deep tawny-orange color; this condition is accompanied by depressed spirits, intellectual torpor, loss of appetite, general debility, and uneasy sensations over the region of the liver and the stomach. Hepatic tenderness is a very variable symptom; enlargement of the liver, as indicated by an increased area of dullness on percussion, is more common. Sometimes there is nausea and vomiting. The stools are usually clay colored, and the bowels constipated, though at times there is diarrhoea. The urine is discolored from the presence of biliary matters. Very often the patient is so debilitated as to be quite unfit for duty, though not usually confined to his bed; at other times, however, he continues to perform service throughout the affection.

"After lasting a variable period, the symptoms slowly subside and the patient is gradually restored to health, the mental torpor and debility persisting often some time after the icteroid hue has disappeared. The first symptom of amendment is generally a change in the color of the stools, which gradually resume their normal appearance. Cases occasionally occur of a graver character than indicated above, the symptoms of biliary toxemia being aggravated to stupor or even coma, and such cases at times prove fatal."

This description of the epidemic of 1862 gives a good picture of the epidemics of the past few years.

In the usual benign, nonfatal case three distinct stages may be recognized: an initial, preicteric stage of several days, an inter-

mediate, icteric stage of from 2 to 3 weeks, and convalescence lasting from 1 to 2 months. Occasionally the disease is more protracted. The initial manifestations are subject to variation but usually follow one of two characteristic patterns. The disease may be ushered in abruptly by symptoms common to many acute infections: fever, chilliness, headache, malaise; or the onset may be more gradual with gastro-intestinal symptoms—anorexia, nausea, and vomiting—predominating. Jaundice also varies considerably in degree as well as in duration; in fact, in many cases jaundice is extremely slight or entirely absent. Early in the icteric stage the liver is usually enlarged and often tender. The spleen is slightly palpable in approximately one fourth of the cases; the temperature is normal; there is often a mild leukopenia. Several biochemical facts indicate impairment of some of the functions of the liver, but there is no test which measures the severity of the lesions nor is specific for the disease. Convalescence begins when jaundice gradually fades and the symptoms disappear.

This brief sketch applies to the average case which goes on to uneventful recovery. But in approximately 0.3 per cent the disease ends fatally. Initially there are no clinical differences between nonfatal and fatal cases. Seldom in the intermediate stage is there evidence that the disease is running other than its usual benign course; many patients are ambulatory and appear to be steadily improving. Then suddenly a dramatic change occurs. The patient becomes drowsy, listless, stuporous, and finally comatose; or, on the contrary, he becomes restless, excited, or delirious; frequently these nervous manifestations alternate. Certain deep and superficial reflexes are exaggerated; often the speech is scanning and there is marked muscular weakness. The temperature, which has been normal, rises sharply toward the end. Signs of ascites may become evident. The appearance of the nervous manifestations usually heralds the final stage, with death occurring within 10 days.

Pathologic Anatomy

It is convenient to discuss, first, the lesions in the liver found in the non-fatal cases; second, the structure of the liver after clinical recovery from hepatitis; third, the change in the liver and in other organs that characterize the fatal cases which run a subacute course; and finally, the lesions of the fulminant form. The discussion of the microscopic alterations may be aided by considering them in reference to the unit of hepatic structure and of function: the lobule. Let me recall to you that each lobule is a miniature liver, and possesses all the structural and functional components of the organ as a whole. In discussing the pathologic anatomy of any hepatic lesion we must answer the following questions: Are all the lobules involved? If so, are all lobules affected to an equal degree? Are the lobules involved diffusely or zonally? What parts of the lobule are injured? What kind of injury is manifest, and what is the nature of the reaction?

The Lesions of Non-fatal Hepatitis. The first systematic study of hepatitis by aspiration liver biopsy was published by the Danish investigators, Roholm and Iversen in 1939. This was followed by larger series reported by Dible, McMichael and Sherlock in England, and by Axenfeld and Brass in Germany. An extensive investigation by Horan, Jolliffe and Mallory, based upon 160 peritoneoscopic biopsies has not as yet been reported in full, though a preliminary account has been given by Mallory. This study is especially valuable because most of the patients had a relatively mild attack, and in a considerable number, biopsy examinations were made in the early, pre-icteric stage of hepatitis. In all four of these series it has been found that the lesions are similar in kind but dissimilar in degree to those of fatal cases. They consist essentially of destruction of liver cells and an associated inflammatory reaction. The extent of the destructive process varies widely. In the milder cases there may be loss of only scattered cells. The severity of the lesion however may

be much greater; for example in the series reported by Dible and his associates it was estimated that in 12 out of 56 cases more than half of the liver cells were damaged or destroyed. The injury is usually most manifest in the central zone of the lobules. The lesions are accompanied by dilatation of the bile canaliculi with prominent plugs of bile. The degree of intralobular retention of bile is as variable as the degree of clinical jaundice. Cell damage is accompanied by an inflammatory reaction, chiefly mononuclear in kind, and usually most pronounced at the lobular peripheries, although foci of intralobular inflammation are not infrequent. The sinusoids and the reticulum remain intact; the damage affects specifically the hepatic cells. Those that are killed rapidly undergo autolysis, and the remaining uninjured cells quickly multiply so that the damage is repaired quickly.

Mallory and others have presented evidence that in patients without clinical development of jaundice, the hepatic lesions are quite similar to those found in patients having jaundice.

All observers agree that no histologic criteria have been found by which the sporadic form of hepatitis may be distinguished from the epidemic form, nor can the lesions of the naturally occurring disease be differentiated from those of inoculation hepatitis.

To the wealth of information furnished by these investigations based on biopsy of liver (which of necessity permits study of only a very small fraction of the organ), some facts of significance have been added by postmortem examinations of patients who have died from an unrelated disease or from trauma during an attack of a hepatitis which itself would in all probability have pursued a benign course. These studies have made it certain that every lobule throughout the entire liver is affected, and that in the great majority of cases the degree of lobular involvement is approximately uniform throughout the organ.

The Structure of the Liver after Clinical Recovery from Hepatitis. Of paramount importance are the questions: what lesions, if any, remain in the liver after the patient has been restored to health? Does the liver, when studied microscopically, show evidence of permanent damage, or, on the contrary, is repair complete, is lost tissue replaced, does healing occur without scarring? The answer to these questions has been obtained through two lines of investigation: first, through the study of biopsy material obtained both during the active stages of the disease and after clinical recovery; second through postmortem examinations of livers from patients who had recovered from a typical attack of epidemic hepatitis, and who died later as the result of trauma or of an unrelated disease. The biopsy series have furnished proof that in the great majority of cases the damage is repaired quickly and completely. The postmortem studies have led to a similar conclusion. We have studied livers of approximately thirty patients who had passed through typical attacks of every degree of severity, and of duration ranging from 2 weeks to 6 months. The interval between discharge from hospital and death from unrelated cause varied from 1 week to over 3 years. In all instances the liver was grossly normal. Microscopically, there was, in all cases examined 2 months or more after recovery, complete restoration of the parenchyma; in none, any distortion of lobular architecture, and in none any indication of a progressive process. It is inferred that complete restoration of the liver occurs in the vast majority of non-fatal cases of hepatitis; that as a rule, an attack of hepatitis will not be followed by untoward after-effects of progressive nature. These conclusions are in harmony with the well known great powers of hepatic regeneration. Experiments have amply demonstrated that as long as damage is confined to the liver cells themselves, and as long as the damage is not repeated at short intervals, the destroyed parenchyma will be replaced rapidly through regenerative multiplication of the cells which remain intact. All evidence points to the fact that there is no relation between epidemic hepatitis and the most common form of human cirrhosis, the

Laennec's type. It is conceivable, though not proved, that a chronic cholangio-hepatitis ("Hanot's cirrhosis") may arise as the result of a complicating infection of the intrahepatic biliary system during or after the course of an attack of hepatitis. This type of cirrhosis is so rare as to make a possible causal relation to hepatitis of little more than academic interest.

The Subacute Fatal Form of Hepatitis. When hepatitis terminates fatally, the survival period, in most endemic or epidemic cases reported until recently, ranges from 4 to 6 weeks. In our series of over 300 cases, studied at the Army Institute of Pathology, only 3 per cent of fatalities occurred after 100 days. In every instance of fatal hepatitis the liver is the site of the principal lesions. The gross appearance of the organ is almost pathognomonic. Usually it is reduced in size, and weighs between 800 and 1200 gms. Less often shrinkage is greater, or on the contrary the liver is enlarged. The organ is deformed, as the surface in some areas is finely wrinkled, smooth, or sunken in, whereas elsewhere coarse nodules or tumor-like masses project.

The irregular distribution of the lesions is even more conspicuous on the cut surface; large, red, meatlike areas, which ooze blood and in which the landmarks are obliterated, alternate with pale, ivory-colored or greenish nodular patches which are decidedly ischemic. Upon microscopic examination one finds that in the red areas the liver cells have disappeared completely, but, as in the more acute cases, the reticular framework is preserved and the sinusoids are engorged. Often the intima of the efferent veins is densely infiltrated with inflammatory cells. This endophlebitis may be accompanied by thrombosis. An inflammatory reaction of the same kind as in the acute cases, though less severe, invariably exists in the lobular remnants and the interlobular stroma. Proliferating small bile ducts usually outline the "skeletons" of the lobules.

When destruction of the liver cells is incomplete, new parenchyma forms rapidly through regenerative hyperplasia of the surviving cells. The process of attempted restoration begins early, and within 2 or 3 weeks large nodular or tumor-like masses of new tissue have been built. The new parenchyma is often arranged in an atypical pattern; it rarely has a normal lobular structure or proper connections with afferent and efferent vessels and with the biliary system. In some areas the cells form giant tubules or broad sheets of multinucleated syncytia, which resemble neoplastic rather than regenerative growths. Where the cells have formed hepatic columns the canaliculi usually are obstructed with masses of bile, and the liver cells themselves contain coarse granules of bile. It seems unlikely that such atypical tissue is functionally adequate.

Besides regenerative phenomena in the liver cells there are proliferative changes in the small interlobular and perilobular (septal) bile ducts. Here, also, hyperplasia begins early and progresses rapidly through budding and branching. It has long been debated whether biliary epithelium can be transformed into liver cells; hence, whether, through primary regeneration of bile ducts, destroyed hepatic parenchyma can be restored, or whether, on the other hand, the new parenchyma is formed exclusively from preexisting liver cells. It is true that one frequently encounters structures which suggest transformation of proliferated bile ducts to liver cells. But such a differentiation cannot be postulated on morphologic grounds alone, and in any case it would contribute little to the restoration of hepatic tissue. It remains to state that the larger intrahepatic bile ducts are normal and that scarring is absent or inconspicuous both in the areas of complete parenchymatous destruction and in the regenerated portions.

The Fulminant Form of Fatal Hepatitis. During the past 3 years the course of epidemic hepatitis has frequently tended to be fulminant. Thus in a series of 196 fatal cases which occurred in the U. S. Army between August 1943 and April 1945 and were studied by Mallory and myself at the Army Institute of

Pathology, over half terminated fatally in less than 10 days. In contrast, in another Army series of 125 fatal cases from the epidemics of 1942 and early 1943 there was not a single case of such fulminant type. The pathologic anatomy of the liver in these rapidly fatal cases differs greatly from the changes characteristic of the subacute form which has been described in the preceding section.

When death occurs within 10 days the liver usually is reduced in size, but in only one-third of the cases does the weight fall below 1000 gm. Reduction in size is not invariable; in 20 per cent the weight of the liver is actually greater than normal. The organ is soft and flabby in consistency; its surface is smooth or slightly wrinkled; its color varies from dark brown to purplish-red. The cut surface shows uniform involvement, but examination by the naked eye reveals no characteristic pattern nor any indication of the degree of parenchymatous destruction. There is often an exaggerated "nutmeg" mottling, and at times the landmarks are so indistinct that the organ has the appearance of an acutely congested spleen.

Two processes dominate the microscopic picture: extensive destruction of liver cells and marked inflammatory reaction. Usually all but narrow rims of cells at the lobular peripheries are destroyed; often scarcely a single liver cell remains. The dead cells are removed rapidly and all traces of debris disappear within a few days. This massive destruction is limited specifically to the liver cells, the reticulum remains intact. The sinusoids are preserved; usually they are widely distended with blood, but although hemorrhages may occur they are not the rule. The destruction of hepatic parenchyma is associated with inflammatory infiltration of cells most conspicuous at the lobular peripheries, that is to say in the portal stroma and in the normally vague interlobular boundaries. The cells are chiefly mononuclear forms—reticulo-endothelial derivatives, lymphocytes, and plasma cells—but neutrophils and occasional eosinophils also are present. Within the lobular remnants where the inflammation is less prominent, mobilized and proliferated macrophages predominate. These cells commonly have engulfed a brownish pigment, lipofuscin, which is probably derived from the disintegrated hepatic parenchyma. The minute interlobular bile ducts usually show some evidence of early proliferation. In brief, the liver in the most fulminant cases of hepatitis is reduced to a spongy framework infiltrated by inflammatory cells and distended with blood.

Extra-hepatic Lesions in Fatal Cases of Hepatitis. Although the pathologic changes which take place are most prominent in the liver, they are by no means limited to that organ. One of the most striking features of fatal epidemic hepatitis is ascites. In cases having a survival period of less than 10 days ascites is encountered in approximately 25 per cent; when the survival period exceeds 10 days the incidence rises to 70 per cent. The fluid usually is large in amount, is nearly always tinged with bile, and often with blood. There is no correlation of ascites with size of the liver; it occurs as frequently when the liver is greatly shrunken as when it is of normal size or enlarged. In approximately one-fourth of the cases there is accompanying pleural effusion, and in half, slight edema of the ankles. The clinical records indicate that ascites precedes ankle edema, which in these cases is probably due to mechanical interference with venous return.

The gall bladder and extrahepatic ducts are without significant changes. The regional lymph nodes of the liver, and often the mesenteric nodes, are swollen and edematous. The spleen is moderately enlarged in three-fourths of the cases. Its microscopic appearance varies with the duration of the disease; in relatively early cases there is hyperplasia of lymphoid and reticulo-endothelial cells; often there are minute foci of necrosis. In later stages the picture is that of portal hypertension. In the gastrointestinal tract lesions of several kinds are encountered. Erosions are common in the lower third of the esophagus probably as the result of persistent vomiting. The small and large intestines are frequently

edematous. In approximately 15 per cent of the cases with a subacute course the cecum is the site of marked phlegmonous inflammation which probably develops during the last few days of life, to judge from the infiltrating cells which are always well preserved.

Hemorrhages, common in epidemic hepatitis, are most conspicuous along the attachment of the gut to the mesentery, in the mesocolon, the mucosa of the intestines, and the bronchial walls, throughout the pulmonary tissue proper, in the epicardium, the endocardium, and the pelvis of the kidney. They are found more rarely in other organs and almost never in the brain and the adrenals. The hemorrhagic phenomena of epidemic hepatitis are doubtless due to disturbances in prothrombin formation in the damaged liver, but this does not explain their selective location.

In the majority of cases the kidneys are moderately enlarged and flaccid. When the survival period is less than 10 days the microscopic changes are those of fat storage in the proximal convoluted tubules and the ascending limb of Henle. Significant degenerative lesions are lacking. In the more subacute form of the disease the changes correspond to those of so-called cholemic nephrosis which range from simple "cloudy swelling" to actual necrosis.

Despite the striking cerebral manifestations that are characteristic of the final stage of hepatitis, the brain shows little alteration. Ganglion cells here and there present nonspecific, microscopic changes, such as swelling, distortion, and loss of nuclear detail. In a small proportion of cases perivascular and occasionally more diffuse inflammatory reactions are found, especially in the hypothalamus. The meninges may be the site of similar manifestations.

Pathologic Physiology and Clinico-pathologic Correlations

There are many aspects of the pathologic physiology and of clinico-pathologic correlations worthy of discussion, but only a few can here be chosen for comment.

Disparity between the Clinical Duration and the Probable Age of Lesions. A disparity between clinical and anatomic duration of epidemic hepatitis is often obvious. Those who have studied biopsy specimens have frequently observed profound changes in the liver although the patient has been ill but a day or two. Similarily, in many instances although death occurred a few days after the onset of symptoms, the liver showed extensive inflammatory reaction and considerable proliferation of the small bile ducts, or conspicuous regeneration of the hepatic parenchyma. It is not credible that such changes could have occurred in the brief time suggested by the clinical story. It may be concluded that the lesions are often older than the clinical manifestations. In other words, when symptoms appear the liver may already be involved extensively. In fact in some instances the clinical course may be "silent" or the symptoms minimal even in patients which die within a few days.

Jaundice. The mechanism of jaundice is complex. In biopsy specimens as well as in the livers from fatal cases, the larger bile ducts (including those in the portal triads) are unobstructed, but many of the intralobular canaliculi are occluded with plugs of bile. It seems probable that such mechanical and intralobular obstruction to bile flow is an important factor in the mechanism of jaundice. Another factor however, plays a part: the liver cells themselves are damaged, and in the more severe cases, many are destroyed; indeed, when the disease is fulminant every single liver cell may be removed. Damage or destruction of the hepatic parenchyma will obviously make it impossible to take up and transport the bilirubin brought to the liver by the circulating blood.

Duration or degree of jaundice is not a measure of the severity of hepatic involvement. That hepatitis in its usual benign form often has a completely anicteric course has already been stated; we must assume that in such cases damage of the liver cell or obstruction in the canaliculi is of slight degree. More difficult is the explanation of the occasional fulminant

cases of hepatitis without jaundice. Perhaps it requires a longer time than we generally believe for jaundice to develop.

Ascites. The mechanism of ascites is also complex, but at least it is recognized that two principal factors involved are (a) alteration of the plasma proteins leading to lowering of the colloid osmotic pressure and (b) an interference with the blood flow through the liver. Frequently in epidemic hepatitis, ascites appears at a time when plasma proteins show little alteration, but in many instances there are profound disturbances of the blood flow through the liver; the organ in some areas is overloaded with blood, elsewhere it may be ischemic. It seems plausible, therefore, that mechanical interference with blood flow is one of the chief causes of the ascites of hepatitis.

The Problem of the So-called Hepato-renal Syndrome. Of the many ill-defined terms in common usage, the term "hepato-renal syndrome" is one of the vaguest. To some, and perhaps the majority, it means renal damage consequent to liver injury, the kidney damage being so severe that it leads to uremic death. To others, it includes all forms and degrees of simultaneous impairment of both liver and kidney.

That there are many agents which may damage both the liver and kidney concomitantly, is a fact which requires no discussion. But it is worthy of inquiry whether primary damage to the liver can secondarily involve the kidney. Two hypotheses have repeatedly been suggested by those who have defended the existence of a hepato-renal syndrome in the sense here used: (a) that a nephrotoxic substance is elaborated by the sudden destruction of liver parenchyma, and (b) that a severely damaged liver fails to detoxify an unknown nephrotoxic agent from some other source. If either of these hypotheses were correct, fulminant hepatitis, with its massive and rapid destruction of liver cells should prove a good example of the hepato-renal syndrome. But, in the fulminant cases of hepatitis there were but very rarely any significant disturbances either of function or of structure of the kidney. Such changes as did occur were purely transitory in character. Only when the disease was accompanied by profound shock did grave renal disturbances develop; they were of the kind characteristic of the lower nephron nephrosis, and led to renal insufficiency. But this condition is not elicited by liver disease or liver injury as such; it may develop after severe crushing of muscles, after extensive trauma to any part, after mismatched transfusions of blood, and after a great variety of poisons. It would seem best to drop the term "hepato-renal syndrome", for the experiences during the past war have made it plain that injury or disease of the liver plays no specific part in renal damage.

Factors Responsible for Fatal Hepatitis. Hepatitis usually is a benign disease. In the non-fatal form the amount of liver parenchyma destroyed is no more than can be promptly restored by regenerative proliferation. But in the fatal form there may be such massive necrosis as to make restoration an impossibility. The extent of this destruction varies; at times the entire parenchyma is lost, resulting in death within a few days; oftener, massive destruction is confined to certain areas though elsewhere cells survive in sufficient numbers to form great nodules or tumor-like masses of parenchyma. Thus life may be prolonged for weeks or months.

There is no fundamental difference in the nature of lesions of the non-fatal and the fatal form of hepatitis; all possible degrees of destruction and completeness of restoration may occur.

In the non-fatal form the injurious factor is, in all probability, the virus itself. But does virus activity alone account for the more massive destruction characteristic of the fatal form; or are there other "conditioning" factors? We have a suggested parallelism in the effect of a number of industrial poisons, such as various chlorinated hydrocarbons which may effect, on the one hand, little or insignificant damage to the liver, and, on the other hand, produce extensive necrosis. Some of

these compounds are widely used in industry; but the incidence of massive necrosis ("acute yellow atrophy") in workers exposed to these compounds is very low. This fact suggests either that certain individuals are more susceptible, or that in fatal cases liver damage has been "conditioned" or augmented by some other agent or agents. That the latter supposition is probably correct has been shown by experiment: several investigators have implicated improper or inadequate diet, and poor nutritional states as increasing the susceptibility of the liver to either chemical poisons or to the virus of hepatitis. It seems very likely that host factors of the kinds mentioned, rather than increased virulence of virus are the factors responsible for a fatal outcome in hepatitis.

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Development of Plastic Surgery as a Specialty in the United States*

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THIS branch of surgery has only comparatively recently attained recognition as a definite specialty, although it has been practised by surgeons from the most ancient times. In the minds of many of the laity plastic surgery means the alteration of God-given features for the improvement of appearance, but it includes a great deal more than this. It deals with the correction of congenital and acquired defects and deformities not only of the face but of all parts of the body by the shifting and transplantation of tissues for the improvement of function, appearance, contour and comfort of the patient. Thus it is evident that plastic surgery touches and overlaps many other special fields of surgery, such as orthopedic surgery, neurologic surgery, urology, ophthalmology and otolaryngology. The branch of plastic surgery known as maxillofacial surgery overlaps the field of dentistry.

I will not go at length into the history of plastic surgery, since this has been well covered by J. Staige Davis, Aufricht, and others (1, 2, 3), but will mention a few important landmarks bearing on the development of the specialty in this country. At the outbreak of World War I there was no recognized specialty of plastic surgery. Most general surgeons performed reparative operations, while a few took a special interest in them. In addition, there was a considerable number of "oral" surgeons, such as Brophy, Gilmer, Cryer, Marshall, G. V. I. Brown and Chalmers J. Lyons, who were not general surgeons, but who by reason of their dental training took a special interest in surgical diseases of the mouth and jaws, particularly cleft lip and palate. At the outset of World War I, Great Britain and France were confronted with the care of many injuries of the face and jaws, and were at first greatly handicapped by the lack of experienced surgeons and dentists. As time went on, however, native ability of certain men came to the fore and efficient organizations for the care of these cases were set up. In France, several maxillofacial centers were established, headed by such men as Morestin, at the Val-de-Grace in Paris, Lemaitre at Vichy, Pont at Lyon, and many others. Georges Vilain, of the École Dentaire of Paris, is noteworthy for the development of appliances for fixation of gunshot fractures of the jaws. Two American dentists who had practised for years in Paris—Davenport and Hayes—did outstanding work in the care of jaw fractures in wounded French soldiers at the American Hospital. In England, Gillies and his colleagues from Canada, Australia and New Zealand—Waldron, Risdon, Newland and Pickerill, organized the justly-famed Queen's Hospital at Sidcup for the care of face and jaw injuries. Among other outstanding British workers were Percival Cole, Colyer, Kilner, and Kelsey Fry. Most valuable help was early afforded British face and jaw casualties in France by Kazanjian, of the Harvard Base Hospital Unit, attached to the British before entry of the United States into the War. With our entry into the War in 1917, Surgeon General Gorgas organized, under the Division of Surgery, certain Sections in the Surgeon General's Office, among them a Section on Head Surgery, which included sub-Sections on Ophthalmology, Otolaryngology, Brain Surgery, and Oral and Plastic Surgery. Dr. Vilray P. Blair, of St. Louis, a recognized general surgeon with a special leaning toward surgery of the head and neck, was called to organize the sub-Section and I was fortunate enough to be chosen by him as his assistant. The chief problem presented was to find, train

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and assign a sufficient number of surgeons and dental surgeons to the many hospital units to care for face and jaw injuries. This was no easy task, since there was at that time no organization of the specialty and very few men were known to be proficient in this field. Blair conceived the idea of setting up teams, each consisting of a sound general surgeon and a good dental surgeon who could pool their respective talents as bearing on each case and thus obtain the most favorable results. To instill certain fundamental principles, officers intended for assignment to the work were sent to special short courses of instruction set up at several civilian medical and dental schools. Great help in the selection of dental officers was given by Colonel W. H. G. Logan, Chief of the Dental Division. At the same time, a revised edition of Blair's text-book—"Surgery and Diseases of the Mouth and Jaws"—was prepared and distributed to Army hospitals and individuals assigned to the work. Advantage was taken of experience already gained by colleagues among our allies overseas, and abstracts of papers published by them were prepared and distributed.

When the time came for the dispatch of our hospital units overseas arrangements were made for the assignment of picked American officers for short periods of observation and training at British and French hospital centers where they could see at first hand what was being done for these special cases, before being put on their own responsibility. Thus, the Americans had the advantage of profiting by the experience of their colleagues who had had to start from scratch, and were given the opportunity of avoiding mistakes that had been made. Attempts at segregation of special casualties were made in France, notably in the case of face and jaw injuries at Vichy, where a hospital—Base Hospital 115—specially equipped and staffed for the treatment of head injuries was established. Most of the doctors in this hospital were specialists in ophthalmology, otolaryngology, neurosurgery or surgery of the face and jaws. During crises, like the battle of the Argonne, when all kinds of casualties had to be admitted, the special nature of the hospital had to be suspended for the time being. During one particularly strenuous night, a ward surgeon, who in civilian life limited his practice to ophthalmology, telephoned down to the admitting officer "For God's sake, Henry, don't send me any more arms and legs; I haven't seen a leg, except socially, for fifteen years."

The care given these cases overseas was in general more or less preparatory to the definitive treatment to be received after return to the United States. Certain definite principles were laid down for the early care of face and jaw injuries which, if carried out overseas, very greatly shortened and simplified the treatment after return to the United States. It is to be noted that these same principles held good in World War II.

In this country, three centers were set up where most of the face and jaw injuries were sent on arrival from overseas. These were: General Hospital #11, Cape May, N. J., General Hospital #2, Fort McHenry, Md., and Walter Reed General Hospital, Washington, D. C. Later, two other centers were established, at Columbus Barracks, Ohio, and Jefferson Barracks, Missouri, as convenient locations for continuation of the work by some of the surgeons after discharge from the service. At the Walter Reed Hospital I was fortunate enough to be placed in charge of the maxillofacial service during most of 1919, and had the very able collaboration of Dr. Joseph D. Eby, now an eminent orthodontist practising in New York. After discharge from the Army and return to practice in Philadelphia late in 1919, I continued to visit the Walter Reed Hospital at frequent intervals as consultant almost up to the beginning of World War II. I attribute what little success I have attained in the practice of plastic surgery in large measure to the opportunities placed in my way by Dr. Vilray P. Blair while in the military service, and I wish here to acknowledge my great indebtedness to him.

With the close of World War I plastic surgery as an organized specialty began to gain

momentum. The first indication of this was the formation of a special society in 1921, named the American Association of Oral and Plastic Surgeons, now known as the American Association of Plastic Surgeons. It started as a small, primarily clinical society, consisting of a group of men in different cities, interested in traveling to see the work of other members. This Society now is limited to 60 active members, about 15 senior members and 5 honorary members. We have a three or four day meeting every year, and last May in Nashville and Memphis were honored by the presence of Sir Harold Gillies and five other British colleagues, as well as visitors from several foreign countries. In 1931 a group of New York men organized another society, the Society of Plastic and Reconstructive Surgery, which later (1941) became national in scope. This Society also has an annual three or four day meeting, at which excellent papers are presented. The membership is somewhat larger than that of the Association, but many men now belong to both. For several years the Society published its Transactions, but in 1946 there appeared the first numbers of a bi-monthly journal sponsored by it—"Plastic and Reconstructive Surgery"—with the late Warren B. Davis, of this city, as Editor-in-Chief. The premature loss of such an able director in this enterprise is keenly felt, but we hope to carry on the work he started so auspiciously.

The culmination of recognition of our specialty came in 1938, when the Advisory Board of Medical Specialties of the American Medical Association, with the blessing of the American Board of Surgery authorized the organization of the American Board of Plastic Surgery, for the certification of specialists in this field. Here again, credit is due in very large measure to Vilray P. Blair who spent an enormous amount of time and energy in all matters relating to organization of the Board. Up to the last meeting of the American Board of Plastic Surgery in September, 1947, 174 persons had been certified, 16 of whom have died, leaving a net of 158 active diplomates. There are about twenty individuals now in various stages of consideration by the Board, and many other men undergoing training which will qualify them for eventual certification. Requirements for certification examination are: after graduation in medicine—one year's internship, followed by two years' general surgical residency, two years' sponsored training in plastic surgery and two years of practice in the specialty.

The imminence of World War II found the country better prepared medically and surgically than prior to World War I in every field, including that of plastic surgery. Between the two wars, many advances had been made in the art, especially in the technic of skin grafting and tissue transplantation, and many excellent surgeons had been trained throughout the country, notably at the clinics of Blair and his colleagues at St. Louis, Staige Davis at Baltimore, Ferris Smith at Grand Rapids, Padgett at Kansas City, Gordon New at the Mayo Clinic and Jerome Webster in New York, to mention only a few. The development of antibiotics, blood transfusion and other adjuvants to surgery were of tremendous aid to the technical achievements of the surgeons. As far as plastic surgery is concerned, the successful results of treatment of our wounded in World War II have been largely due to the advances made in civilian practice during the preceding years.

World War II proved the value of this specialty in both military and civilian practice. The necessity for its inclusion in the military organization was evidenced by the selection in 1940 of a plastic surgeon as a member of the Committee on Surgery of the National Research Council and the formation of a Subcommittee of Plastic and Maxillofacial Surgery. The function of these committees and Subcommittees was to advise the Surgeons General of the Army, Navy and Public Health Service on matters relating to the various specialties of medicine and surgery. It is not necessary to give details of the achievements of plastic surgery in World War II. I can only call attention to the very many casualties occurring in this field, requiring years of care in

rehabilitation, and the number of experienced surgeons necessary to carry on this work. In May and June, 1945, Dr. Jerome Webster and I were sent as civilian consultants by the Surgeon General on a tour of inspection and observation to the nine Army centers where plastic surgery cases were being treated. The average number of cases on the plastic surgery service at each of these hospitals at that time was well over 1000, about two-thirds general plastic and one-third maxillofacial. The general quality of the work being done was excellent, in spite of handicaps of limited personnel, equipment and other facilities in many instances. The work at one center near Philadelphia, namely the Valley Forge General Hospital, was particularly meritorious, under the able direction of Colonel James Barrett Brown of St. Louis, who was later made Chief Consultant for all Army Centers. Owing to the volume of work, officers on the plastic surgery service were "frozen", i.e. held in the Army long after specialists in most other fields had been released, and many officers with as many as four years of military service are still being kept from desired return to civilian life. The highest praise is due these men for the cheerful sacrifices they are making for the better rehabilitation of our wounded.

While more closely in touch with the Army, Dr. Webster and I had an opportunity to observe unofficially the plastic surgery at some of the Naval Hospitals. It struck us that the Navy was rather more fortunate than the Army in the provision of facilities and personnel for carrying out the work. There were generous supplies and technicians for making both still and motion pictures of cases, which facilities were rather deficient in many of the Army Centers. The Navy cases were fewer in proportion to the number of trained surgeons so that the feeling of stress so prevalent in the Army Centers was not so evident in the Naval Hospitals. All of these factors contributed to the uniformly excellent surgery seen in these hospitals.

Civilian hospitals throughout the country are gradually becoming conscious of plastic surgery as a specialty and the time is at hand when every large hospital will have a service of this kind. Philadelphia is particularly fortunate in this respect, having plastic surgery services functioning at Jefferson, Graduate, University, Presbyterian, Oncologic, Lankenau, Philadelphia General, Hahnemann and Abington Memorial Hospitals. In several of these teaching hospitals residencies in the specialty have been established for the training of young men in plastic surgery.

I hope I will be forgiven if I have included much of a personal nature in this brief account. I appreciate very greatly the honor you have done me, and fully realize that in honoring me you are according deserved recognition to the specialty which I humbly represent.

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The Bile Pigments and Porphyrins in Jaundice and Liver Disease*

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LOOKING back over the history of the Nathan Lewis Hatfield Lectureship, I have gained a keener appreciation of my own privilege this evening, in considering the distinguished company of scholars which has preceded me on this occasion. I am indeed grateful to the College for the honor of being invited to deliver the 32d Hatfield Lecture.

I shall strive to tell you something this evening, both of the fundamental and clinical aspects of certain hemoglobin derivatives and related substances. Without dwelling more than briefly on details of their chemistry, I should like to speak about hematin, bilirubin, urobilinogen, and the coproporphyrins, with particular reference to alterations in various forms of jaundice and liver disease.

It is well known that hemoglobin is a ferrous-protoporphyrin-globin complex. Porphyrins are substances composed of a "porphin" ring of four pyrrol nuclei connected by CH or methene bridges, each nucleus in turn being a five membered ring with four carbons and a nitrogen at the apex. Protoporphyrin is a divinyl, dipropionic, tetramethyl porphin (1). The prefix "proto-" simply refers to the wide representation of this porphyrin in the body, since it is also the pigment fraction, or prosthetic group of such important respiratory substances as cytochrome and catalase. The available evidence indicates that four molecules of ferrous protoporphyrin, also known as heme, are attached to one molecule of globin (2). This protein has approximately the same molecular weight as albumin (60–70,000) and behaves similarly in a number of other respects, although it is not identical. Protoporphyrin is very similar in structure to bilirubin, the only difference being that it has an additional CH bridge which serves to make a ring of its four pyrrol nuclei. Bilirubin has 33 rather than 34 carbon atoms. It lacks the additional α methene bridge and hence is a chain rather than a ring of four pyrrol nuclei. The matter of the splitting out of this bridge is of considerable significance in the transition from hemoglobin to bile pigment, and I shall return to it in a few moments. First, however, it would be well to give some

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consideration to hematin. The chemical treatment of hemoglobin in vitro, as for example, by dilute acid, yields hematin, a ferric complex of protoporphyrin. In fact, the ease with which hematin is formed in the test tube undoubtedly promoted the view which was generally held for many years that hematin is intermediary between hemoglobin and bile pigment in vivo, and that the globin is first removed and the iron then split out after which the protoporphyrin ring opens to yield bilirubin. The results of more recent studies indicate, however, that hematin is formed only under abnormal circumstances, and especially in the presence of hemolysis associated with liver injury, as in gas bacillus and certain other septicemias, in blackwater fever, in pernicious anemia, in severe relapse, or in cases of cirrhosis or hepatitis with hemolytic anemia (3, 4, 5, 6). The hematinemia of these conditions is usually associated with hyperbilirubinemia. This is especially true of certain cases of macrocytic hemolytic anemia occurring in association with advanced hepatic insufficiency. Hematinemia may also be isolated, however, as in the pure form of hematin "icterus" (6). This is at times seen when there is a hematoma in an epithelial lined space having access to the blood stream, as for example in the kidney. Hemoglobin is also converted to hematin, at least in part, in many cysts lined by glandular epithelium (6). It should be emphasized that hemoglobin in the gastrointestinal tract is converted to hematin, and in small measure to protoporphyrin, but not to bilirubin. Quite another sequence is observed, however, in spaces lined by cells of mesenchymal origin, as for example, connective tissue, peritoneum, pleural cavity, and subarachnoid space. In these areas, hemoglobin is converted directly to bilirubin and hematin is usually not observed (4, 6). The reticuloendothelial cells, also of mesenchymal origin, as found in the liver, spleen, bone marrow, and lymph nodes, carry out the same conversion of hemoglobin to bilirubin without there being any evidence that hematin is an intermediary. The local formation of bilirubin in extravasations of blood in serous cavities, including the subarachnoid space, is often helpful from a clinical standpoint. In the spinal fluid, the well known xanthochromia is nothing more than a manifestation of such a transition, and it is therefore a faithful indicator of previous bleeding. Bloody fluids from the pleural or peritoneal cavity should be centrifuged to determine by means of the van den Bergh reaction whether the supernatant fluid contains significant amounts of bilirubin, in which event one may conclude that the bleeding had occurred, at least in part, prior to the paracentesis.

In recent years, evidence has accumulated that the transition of hemoglobin to bilirubin is not over hematin but that the first intermediary substance is one in which the porphyrin ring has been opened by a splitting out of the α methene bridge with resultant formation of a biliverdin iron globin or "verdohemoglobin" (7, 8). According to Barkan and Lemberg, and their co-workers, this compound is characterized by an "easily split-off" iron (8, 9, 10). The next step in the transition is the removal of iron after which the biliverdin is reduced to bilirubin by the addition of two hydrogen atoms. From this point the pathway has not been traced with any degree of certainty. Duesberg (4) and Polonovski (11) have suggested that the bilirubin as thus formed in the reticulo-endothelial and mesenchymal cells of the body remains attached to the original globin, the latter being first removed by the liver cells. This is a logical assumption which has not been disproven and may be accepted tentatively, at least until contrary evidence is brought forward. The possibility must also be considered that a certain fraction of the bilirubin becomes detached from the globin to become complexed with another of the serum proteins. Thus it has recently been found that a small amount of bilirubin in normal human serum is bound to the α_1 globulin (12, 13).

Bilirubin in the bile is not attached to protein and is probably the sodium salt, as suggested by Hunter (14). The available

evidence favors the view that the two bilirubins are responsible for the differing van den Bergh reactions, the bilirubinglobin being the slow component whose delayed reaction is greatly speeded up by the addition of alcohol (indirect reaction); the prompt reaction being given by the sodium bilirubinate of the bile (15). The available evidence also indicates, quite in accord with van den Bergh's early views, that when the prompt reaction is given by the blood serum, it points to a regurgitation of bile into the blood, either because of increased permeability of the cholangioles on a chemical or toxic basis, or actual rupture due to increased biliary pressure. In this regard there is considerable indication that the ampullae of the bile capillaries are the point of greatest leakage; Aschoff (16) referred to them as "the Achilles heel of the biliary tract." The presence of a delayed or indirect reacting van den Bergh reaction in the blood serum may well be due to bilirubinglobin provided by the degradation of hemoglobin in reticulo-endothelial or mesenchymal cells. Correlating this with the fundamental classification of jaundice by Rich (17), retention jaundice is characterized by an increase in bilirubinglobin (delayed or indirect reacting van den Bergh), *without* bilirubin in the urine, and regurgitation jaundice by an increase in sodium bilirubinate (prompt reacting van den Bergh), with bilirubinuria. Ducci and I (18) have shown that the quantitative measurement of the serum bilirubin is best divided into a one-minute or prompt direct, and total, the latter measurement being made after sufficient preliminary dilution and addition of alcohol. The measurement of the prompt reacting bilirubin at one minute might seem unduly arbitrary, but careful study has shown that the great majority of the prompt reaction is over at the end of one minute and that after this time, only the slow component (bilirubinglobin) continues to react with the diazo reagent (15). A reaction curve of this type makes it clear that the difference between the two varieties of bilirubin is distinct. If there were but one, a parabolic type of reaction curve would be anticipated rather than the shoulder type which is found. The addition of alcohol at any point along the gradual slope of the slow component quickly converts the delayed to a prompt reaction.

van den Bergh clearly recognized that the prompt or immediate reaction takes place within one minute, but until recent years this fraction was not measured quantitatively. In our material the normal value for the one minute or prompt reacting bilirubin is less than 0.2 mg. per 100 cc., and the total 1.0 mg. per 100 cc. or less (15). It is pertinent to note that all or nearly all of the bilirubin of human fistula bile reacts within one minute. Conversely, nearly all of the serum bilirubin in uncomplicated cases of familial hemolytic jaundice (pure retention jaundice) reacts slowly, after one minute (15).

Transition of the delayed or indirect reacting bilirubin (globin) in the liver cell, or possibly in the Kupffer cell, to the prompt reacting sodium bilirubinate, is believed probable. In cases of diffuse hepatic necrosis, even shortly before death, marked increases of prompt reacting bilirubin in the circulating blood are often observed. This would seem paradoxical if the conversion is accepted as a function of the liver. A similar situation is often encountered in the same cases, however, in respect to the urea nitrogen which may be found considerably elevated even in the presence of outspoken hepatic insufficiency. It may be that the necessary enzyme systems are still available in these livers in spite of the extensive histologic evidence of damage.

The prompt reacting bilirubin, or sodium bilirubinate, gains access to the urine with relative ease, whereas the bilirubinglobin probably does not pass through the glomerulus at least from those concentrations at which it is found in the circulating blood. In this connection, it should be remembered that the renal threshold for hemoglobin, a molecule of approximately the same size, is usually above 100 mg. per 100 c.c. (19), while values of 10–15 mg. of bilirubinglobin are unusually high. Bilirubinuria has not been observed

even at the highest level of delayed or indirect reacting bilirubin, while it is nearly always present when the one minute or prompt reacting bilirubin is even moderately elevated. In this regard, a finding by Neefe and his associates (20) during the recent war was of much interest, i. e., that bilirubin appears in the urine in the pre-icteric stage of hepatitis before the total serum bilirubin has become significantly elevated, even, in fact, while it is still 1.0 mg. per cent or lower. Subsequent studies have made it clear that the renal threshold for the one minute or prompt reacting bilirubin is different at the outset and during the recovery stage of a diffuse liver injury, as for example, infectious hepatitis (15). Thus, in the incipient or pre-icteric stage of the disease, considerable amounts of bilirubin may be found in the urine with elevation of the prompt reacting bilirubin in the serum only to as little as 0.4 mg. per cent; the total being well within the upper limit of normal (15). This undoubtedly accounts for the history so often obtained in these cases of dark urine for several days before the appearance of jaundice or of dark urine in cases with otherwise typical symptoms but without the appearance of jaundice; in other words, hepatitis without jaundice. This phenomenon was well described by George Budd (21) slightly more than 100 years ago, and in fact it appears that Budd was the first to recognize cases of hepatitis without jaundice.

As the serum bilirubin is declining during the later stages of the disease, bilirubin usually disappears from the urine when the serum one minute bilirubin is from 0.8 to 1.2 mg. per c.c., although at times even much higher than this (15). These studies have made it clear that the generally accepted (22, 23) idea of a fixed renal threshold for bilirubin of 2.0 mg. per 100 c.c., must be abandoned. Because bilirubinuria is so commonly a feature of pre-icteric and an-icteric hepatitis, especially during the early stages of the disease, it became clear that a simple and reliable method of testing the urine for bilirubin, suitable to mass application, was much needed. Such a method was developed in collaboration with Roy Turner and Violet Hawkinson (24, 25) and has been designated as the "barium strip" test. Actually this is a modification of the Harrison test for bilirubin in the urine. It is considerably simpler, as it requires only a barium impregnated strip of especially retentive thick filter paper which is held briefly in the urine sample to be tested. The urine runs up the strip by capillary attraction, and any bilirubin present is concentrated at the surface. A drop of Fouchet's reagent (which contains trichloracetic acid and ferric chloride) upon the surface line quickly elicits a green color if bilirubin is present, the intensity of the color being roughly proportional to the amount. Hundreds of urine samples can be run in a short time with this method. It is believed that its use adds materially to the routine urinalysis, since in many instances it quickly gives evidence of latent hepatic functional impairment or of biliary obstruction, thus indicating the direction that further investigation should take.

To return now to the relationship of the principal derivatives of hemoglobin, it may be noted that the bilirubin of the bile is reduced in the colon, first to mesobilirubinogen, and this by a bacterial mechanism as yet unknown, to stercobilinogen (15). These are the chromogens which in the composite constitute urobilinogen and which are responsible for the well-known Ehrlich aldehyde reaction. Fortunately for the quantitative determination of urobilinogen, the intensity of the Ehrlich color reaction with each of these chromogens is identical. Furthermore, there is no reason to believe that one has a different biochemical significance from the other. Each chromogen on dehydrogenation, especially in the light and air, yields an orange-yellow pigment, mesobilirubinogen giving rise to urobilin IX, α, stercobilinogen to stercobilin (6). These twin pigments are responsible in considerable part for the color of the normal feces. Both exhibit intense green fluorescence with zinc salts, the well-known Schlesinger test.

Urobilinogen, that is to say, the composite of the two chromogens, is absorbed in considerable part, usually in the neighborhood of 50

per cent, into the portal blood returning to the liver (6). Under normal circumstances the liver disposes of this fraction rather completely, a very small amount, less than 3.5 mg. per 24 hours, escaping into the general circulation and thence into the urine, and a small fraction returning in the bile to the intestine. It does not appear, however, that the bulk of the reabsorbed urobilinogen is accounted for by these small fractions, and one can only assume that the liver metabolizes and perhaps utilizes urobilinogen in some as yet unknown way. Felix (26) showed, a number of years ago, that if urobilinogen is mixed with liver brei, it quickly disappears and can no longer be detected. The problem of the fate of urobilinogen returning to the liver in the portal circulation requires further study. From a clinical standpoint, however, this fraction has a great deal of interest and importance since, in the presence of liver injury, it is allowed to pass on into the general circulation in varying proportions and its presence in the urine is thus indicative of hepatic functional impairment. In judging of the significance of the presence or absence, and of the amount of urobilinogenuria, several factors must be taken into account, as follows:

1. Complete or high grade interference in the outflow of bile.
2. "Throttling" of blood destruction; diminished formation of bilirubin, and hence of urobilinogen.
3. Diarrhea or other cause of malabsorption from the colon.
4. Renal insufficiency.

Study of the feces and urine urobilinogen permits insight into the rate of blood destruction, or in cases of regurgitation jaundice, into the degree of exclusion of bile from the intestinal tract due to biliary obstruction or cholangiolar injury (27, 28). The normal range of feces urobilinogen is usually from 100–200 mg. per day, probably not exceeding 280 nor less than 40 mg. even in exceptional instances.

In pure retention jaundice, the feces urobilinogen determination is of great help in determining whether the jaundice is primarily hemolytic or rather on the basis of a constitutional hepatic dysfunction (familial non-hemolytic jaundice; icterus intermittens juvenilis). In the latter event, the feces urobilinogen is not increased, while in hemolytic jaundice, or anemia, it is regularly increased and usually to a marked degree.

Regurgitation jaundice is caused at least as frequently by diffuse parenchymal liver disease as by extrahepatic biliary obstruction. From the therapeutic standpoint, therefore, it is not enough to decide simply that a patient has regurgitation jaundice; in other words, to conclude that because the van den Bergh reaction is prompt in type and there is bilirubin in the urine, there is an extrahepatic biliary obstruction, and the patient should be operated on. The urobilinogen excretion is often of value either singly or in association with other observations in determining the nature of the underlying disease, and whether the jaundice is surgical or medical. Thus, if a very large amount of urobilinogen is encountered in the urine, this speaks strongly for a diffuse parenchymal jaundice, either a hepatitis or other type of liver injury.

It should be noted, however, that it may be encountered also with extrahepatic biliary obstruction complicated by obstructive biliary cirrhosis or suppurative cholangitis. A persistent finding of less than 5 mg. of urobilinogen in the feces per day, and of less than 0.5 mg. in the urine is considerably more likely, on a statistical basis, to indicate a cancer involving some part of the extrahepatic biliary tract, more particularly a cancer of the head of the pancreas (28). Some cases of hepatitis exhibit complete exclusion of bile from the intestinal tract for relatively short periods, usually not longer than 8 or 10 days, in rare instances, however, for several weeks. Thus the absence of urobilinogen in the feces and urine is not pathognomonic of cancer. Complete obstruction is observed, too, in occasional cases of common duct calculus, although most of these are incomplete.

The simple qualitative Ehrlich aldehyde test for urobilinogen in the urine is perhaps the only

bedside (laboratory) test of liver function. It is often of the greatest value to the physician who is willing to carry it out himself and more especially to follow it serially. The reagents are stable, can be carried from place to place, and the test takes but a moment. Insofar as the bedside diagnosis of jaundice is concerned, a strongly positive test reveals that bile is entering the intestine and at the same time points toward some degree of diffuse liver injury. A persistently negative test, on the other hand, indicates that little or no bile is entering the intestine and the longer it remains negative in the presence of unrelenting jaundice, the more it points toward an extrahepatic and more likely a malignant cause of biliary obstruction.

During the recent war, and with particular reference to the problem of detecting hepatitis in the earlier stages of the disease, a simple method for quantitating the urine Ehrlich reaction was devised (29, 30). This may be carried out either with a photoelectric colorimeter or with a comparator block suitable for field use. In this method, just as in the simple qualitative test, the Ehrlich reagent is added to the urine in equal parts followed by two volumes of a saturated aqueous solution of sodium acetate. The latter has the virtue of intensifying the color of the Ehrlich aldehyde compound and at the same time minimizing any color reaction due to indol or skatol. For colorimetric purposes, a blank is prepared in which the sodium acetate solution is added first. This prevents the Ehrlich reaction from taking place, but at the same time, provides a control solution containing all of the other disturbing colors in the urine. A series of dilutions of a stable Pontacyl dye standard are used with the comparator block. This simple method is not as specific for urobilinogen as the more elaborate petroleum ether extraction procedure (31, 32). It achieves nothing more than a measurement of the intensity of the Ehrlich reaction, thus eliminating the personal equation and permitting a better evaluation of the test in borderline samples. It is believed preferable to carry out the determination on a 2 hour urine sample collected in the afternoon. Ninety two per cent of 68 normal individuals from whom samples were obtained between 2–4 p.m., were found to excrete less than 1 Ehrlich unit in 2 hours (29). The remainder ranged up to 1.6 units. The procedure is also easily applicable to simple extractions of the feces, and here the method has proven of much value in quickly obtaining information on random samples about the degree of biliary obstruction or the rate of blood destruction. In patients who are very ill, and where accurate collections of feces are impossible, the procurement of as little as 5 grams, if necessary by digital means or enema, readily permits a quantitative Ehrlich determination which may yield decisive information (30).

The simple quantitative Ehrlich procedure as applied to the urine has proven of much value in epidemic hepatitis, especially in the incipient stage, and during the early periods of defervescence. Thus, Hallock and Head (33) found significantly positive tests during the pre-icteric stage in 19 of 20 cases subsequently becoming jaundiced. These individuals were studied during a large epidemic of hepatitis in the Mediterranean theater. 88 per cent of their cases of hepatitis without jaundice showed positive tests. In the cases with outspoken jaundice in our own experience, the urine Ehrlich reaction characteristically becomes negative during the peak of the disease and then it often becomes strongly positive just as the patient begins to improve, gradually diminishing with further convalescence. I believe that activity should not be permitted until the urine Ehrlich reaction has been within normal limits on at least three days. Furthermore, it should be followed as activity is gradually resumed, since if it becomes significantly positive again the degree of activity probably should be restricted for a longer period. It should be emphasized, too, that there are some cases with undoubted persistent activity of hepatitis in which the urine Ehrlich reaction has become negative, and in which other tests such as the bromsulfalein or the urinary coproporphyrin are required to detect residual evidence of impaired liver function. Neverthe-

less it is probable that the patient whose jaundice has disappeared, is in a relatively safe condition if the Ehrlich units per 2 hour urine sample are less than 1.5, on three successive days. In this connection it may be noted that the urine Ehrlich reaction on short period urine samples does not constitute as sensitive a test as the 24 hour urine urobilinogen in mg. In cases where there is doubt as to hepatic functional impairment the 24 hour urobilinogen should be determined. Conversely, little additional information will be gained from the latter, if the simpler test is significantly positive.

The urine Ehrlich procedure, together with the barium strip test for bilirubin in the urine, constitute the only laboratory methods of which I am aware, that the practicing physician may employ at the bedside, in seeking evidence of liver injury or biliary tract disturbance.

Finally, I wish to say a few words about the urinary coproporphyrins in their relation to hepatic and biliary tract disease. There are four coproporphyrin isomers, all of which have been synthesized by Hans Fischer and his associates (1), but only two of these, types I and III, occur in nature. The configuration of the type I isomer differs from that of the protoporphyrin of the heme molecule and it is clear that this isomer is synthesized in the body quite independently of hemoglobin, a process which Fischer termed the "dualism of the porphyrins in nature" (1). The type III coproporphyrin has the same configuration as the protoporphyrin of hemoglobin; nevertheless, much of the available evidence indicates that it too is a product of independent synthesis rather than destruction of hemoglobin (34). Normally, the 24 hour urine in human subjects contains less than 100 gamma of total coproporphyrin (UCP). In a series of 53 normal individuals, it was found that from 60 to 90 per cent of the total is composed of the type I and from 10 to 40 per cent of the type III isomer. The total UCP is rather uniformly increased in cases of liver disease or regurgitation jaundice, whether obstructive or parenchymal in type. In general, the values tend to be somewhat higher when the jaundice is due to diffuse liver disease rather than extrahepatic obstruction but there is too much overlapping to permit any strict separation on this basis. When the degree of jaundice is relatively slight and the UCP markedly increased, a parenchymal type is more likely to be present. The determination of the total UCP has found its greatest usefulness, however, in cases of liver disease without jaundice and in following cases of hepatitis or liver injury after jaundice has disappeared. In the latter group, elevated values have been noted for weeks and often months after the apparent disappearance of the disease. In some the increased value has correlated well with other evidences of increased activity. In others, however, the UCP has remained elevated while all other tests of liver function have returned to normal (34).

The coproporphyrin isomer analysis in cases of jaundice and liver disease has often provided additional information of value and interest. In infectious hepatitis, the increase of the coproporphyrin is uniformly due to the type I isomer (34). This is in remarkable contrast to another virus disease, namely acute poliomyelitis, in which regular increases of type III isomer are encountered in the urine (35). It should be noted that chemical and heavy metal toxicity also characteristically increase the excretion of the type III isomer to a marked degree (34). Whether these various causes of increase are all related in some way to the presence of coproporphyrin III in the central nervous system, as demonstrated by Klüver (36, 37) is as yet unknown. It has been found too that acute alcoholism is quite regularly associated with an increase of coproporphyrin III in the urine. This rather rapidly returns to normal with abstinence. In cases of so-called "alcoholic" cirrhosis, however, the marked increases of coproporphyrin III which are usually observed, often persist for long periods after discontinuance of alcohol. This raises the question as to whether the persistence of the increase is fundamentally related to the causative factors of the cirrhosis. No

information is yet available on this point. In the cirrhosis of non-alcoholic individuals, especially those following infectious hepatitis, the increase of coproporphyrin in the urine is due to the type I isomer, just as it is in infectious hepatitis itself. Thus, there is a fairly strict separation on a biochemical basis, between the primarily fatty cirrhosis of the alcoholic and the non-fatty cirrhosis of other etiology. It will be interesting in the future to study cases of cirrhosis in which chemical or metal toxicity is believed to play an important role; as for example, arsenic, carbon tetrachloride, selenium, and others. While we have not yet had opportunity to accumulate data in such instances, it is clear that arsenic poisoning as well as carbon tetrachloride intoxication, cause a marked increase in the excretion of coproporphyrin III.

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The Prevention of Heart Disease and Disability*

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PREVENTION of other diseases or their cardiac complications in early life, and even in the older age groups, has increased the incidence of cardiovascular diseases due to hypertension and coronary atherosclerosis, by furnishing a large number of susceptible survivors. It is obvious that successful prevention of all deaths from heart disease would result in everyone dying of something else. It has recently been proposed, for example, that chronic alcoholics do not die of coronary disease, partly because they die too young of alcoholism and other diseases (1). This is a blow to those defending the protective value of alcohol.

It is customary to talk very broadly about prevention of degenerative diseases. It is time, however, to remove cardiovascular disease from this category of degenerative diseases and to have a more positive attitude toward prevention.

This paper presents a review of etiologic types of cardiac disease with the purpose of emphasizing the possibilities of prevention by controlling etiologic agents or precipitating mechanisms.

I. Congenital Heart Disease

Taussig (2) in her recent book has considered the possible causes of congenital abnormalities. The first is the hereditary tendency inherent in the germ plasm or the *intrinsic* factor. She quotes Dr. N. J. Eastman who finds that if malformation occurs in one offspring, there is a twenty per cent chance that there will be abnormality of some sort in subsequent offspring of the same mating and a two per cent chance of recurrence of the identical malformation. There are eight out of ten chances, however, that the next child, following one born with a congenital defect, will be normal.

Extrinsic factors are many, but we may note *vitamine deficiencies* during pregnancy as a possibility. Streeter mentions *skeletal abnormalities* in the fetus as influencing the embryonic vascular bed by stress and strain, and Taussig has observed a high incidence of congenital abnormalities of the spine in patients with congenital malformations of the heart. *Syphilis* and fetal *endocarditis* she considers relatively unimportant or non-existent. *Virus infections* are now recognized as of great significance. German measles in the first two months of pregnancy results, in the fetus, in an extremely high incidence of congenital cataracts and malformations of the heart. If the infection occurs in the third month there is an even chance that the infant will be normal. The entire development of the heart occurs in the first two months of fetal life.

The conclusions about the prevention of congenital heart disease at the present time are these:

(1) The reproduction of those with strong hereditary strains of congenital malformations is inadvisable.

(2) Prevention of vitamine deficiency in pregnancy may be important.

(3) Girls should all be encouraged to have German measles in childhood until such time as immunization methods become available. Failing this, extreme precaution should be exercised to prevent exposure of women to rubella during the first three months of pregnancy.

(4) Pregnancy should be interrupted if German measles occurs in the susceptible period.

(5) Further study may show the serious

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nature of other virus infections during this period, but vaccination of the mother for smallpox has been shown to be a safe procedure for the fetus at any stage in pregnancy.

II. Rheumatic Heart Disease

Martin (3) estimates that there are 1,000,000 cases of rheumatic carditis in the United States causing 40,000 deaths a year at the average age of thirty years. Levy, Stroud, and White (4) found rheumatic heart disease responsible for 51% of rejections for heart disease in the draft in Boston, 70% in Chicago, 64% in New York, 70% in Philadelphia, and 40% in San Francisco.

In the United States, however, deaths from rheumatic fever and rheumatic heart disease in the age group, five to twenty-four years, fell from 32.3 per 100,000 in 1917 and 1918 to 9.7 in 1943 according to figures from the Metropolitan Life Insurance Company (5). Each five year period since 1922 has shown a lowered mortality rate and a decrease in percentage and severity of cardiac damage. This, in itself, may not give the entire picture, since it records the results in a selected younger age group.

The predisposing factors for consideration are (6):

(1) *Climate* and *geography*—These are unalterable for practical purposes since most people are restricted to one geographic area.

(2) *Season*—winter and spring being most unfavorable in the temperate zone.

(3) *Social* and *hygienic factors*—including particularly crowding and low income.

(4) *Familial*, *hereditary*, and *constitutional variables*—espoused by Wilson and her colleagues.

(5) *Racial differences*—This is disputed since, for example, rheumatic fever and carditis were about as common in negroes and whites in New Orleans, greater in negroes in Cincinnati, but less in negroes than whites in Philadelphia.

The prominent etiologic factor at present seems to be the unclarified relationship to the hemolytic streptococcus. The virus etiology and the allergic are the other most likely leads.

Conclusions

(1) For an unknown reason rheumatic fever and rheumatic heart disease have become steadily less frequent and less severe in the past twenty-five years. Unanalyzed factors of social and economic nature may be responsible. The voluntary limitation of reproduction at the lower economic levels leads to improved living conditions of children in smaller families. The treatment of streptococcal infections by sulpha drugs, and now by penicillin, may be altering the complicating rheumatic process.

(2) Rheumatic fever and its recrudescences occur in susceptible individuals following hemolytic streptococcus infections, especially in favorable climates. The major emphasis is on the control of such infections:

(*a*) There is a difference of opinion about the value of prophylaxis of rheumatic fever by the use of sulpha drugs. At the present time a small group of our clinic patients has been placed upon a daily dose of 0.75 gm. of sulphamerazine for each seventy-five pounds of body weight. Laboratory control is necessary and blood examinations are made weekly for six weeks, then once a month for three months, and then every three months. Sulphamerazine is preferred because of its slower absorption, permitting a single dose regime, but it may be no more effective than sulphadiazine.

One must remember that sulpha drugs are very dangerous in the treatment of acute rheumatic fever. Furthermore, sulpha prophylaxis is advisable only from October to June and should not be used in individuals exposed to sunlight, or other ultraviolet radiation, because of the dangerous sensitizing effect of the sulpha drugs to actinic radiation. It seems clear that sulpha resistant strains of streptococci may appear in those on sulpha prophylaxis. This is a less important objection than formerly, since penicillin supplies another drug to combat the streptococcus.

(*b*) Experience with penicillin prophylaxis is hopeful. At the House of the Good Samaritan and in private practice we now take routine throat cultures and give penicillin to every rheumatic patient harboring hemolytic streptococci in the throat. Goerner, Massell, and Jones (7) eliminated streptococci from the throats with 10,000 units every two hours for ten days. Tonsillectomy after such therapy has shown the deep tissues of the tonsil free from streptococci on culture. In five of six carriers 150,000 units in oil and wax given once daily intramuscularly for ten days eliminated β-hemolytic streptococci from the throat. Penicillin nose drops and oral penicillin are also effective. This routine is repeated after every respiratory infection. There were no epidemics or recurrences of rheumatic fever in the House of the Good Samaritan in the past year. Milzer, Kohn, and MacLean (8) have recently reported that 1,000,000 units of oral penicillin daily for five days is usually ample to rid the throat of hemolytic streptococci and is a sufficiently large dose to avoid the possibility of penicillin resistance.

(*c*) Coburn and Moore (9) report no recurrences in forty-three rheumatic children in spite of streptococcus infections when two boiled eggs and two frozen egg yolks were added to the daily diet.

(*d*) Occasional good results are reported by the use of streptococcus vaccination in preventing recurrences.

While it seems clear that this prevention or rapid cure of streptococcal infections has a bearing on the prevention of the original initiating mechanism of rheumatic fever, it must be realized, as recently emphasized by Jones, that the progression of rheumatic heart disease has a far less clear relationship to streptococcal infection. There are factors, as yet unknown, which determine cardiac dilatation, progressive valvular disease, and congestive failure, which are operative in certain rheumatic children in whom no evidence of active or latent streptococcal disease can be demonstrated. Prevention of this process, which is indeed the potentially crippling or lethal element in rheumatic fever, needs further investigation.

III. Subacute Bacterial Endocarditis

It is obvious that the control of rheumatic heart disease will be the most effective preventive measure for subacute bacterial endocarditis. Curiously the reverse of this is true, namely that rheumatic heart disease which progresses to severe mitral stenosis and auricular fibrillation is practically a one hundred per cent guarantee of immunity from subacute bacterial endocarditis, as I pointed out in 1930 (10).

Given a susceptible person, that is one with mild rheumatic heart disease, with mitral and aortic regurgitation, one may observe that there are certain precipitating events which commonly initiate subacute bacterial endocarditis, notably respiratory infections and dental extraction. Because of the bacteremia occurring with every dental extraction, even in normal individuals, it is wise to administer penicillin to every rheumatic patient before and just after extraction. We use either 200,000 units by mouth in two doses a few hours before extraction and two 50,000 unit doses after it; or the alternative method of 300,000 units in oil intramuscularly before extraction. There is a difference of opinion as to the economic advisability of this procedure and the dosage of the drug.

We may combine our thinking about rheumatic fever and subacute bacterial endocarditis in relation to penicillin and emphasize a freer use of this drug. At present I feel, in individuals with rheumatic heart disease, that following any respiratory infection, surgical operation, injury, or obstetrical delivery penicillin should be given. It should be controlled by throat cultures and continued, so long as hemolytic streptococci are found. This procedure is statistically of greater importance in preventing rheumatic recurrences, but the routine use of penicillin will probably also prevent invasion of the heart valves by nonhemolytic streptococci.

There is some evidence that transient bacteremia occurs with normal deliveries and it, therefore, seems wise to give penicillin to every rheumatic or congenital cardiac just before delivery and during the puerperium.

Perhaps a word of caution is needed to control enthusiasm for too widespread increase in penicillin prophylaxis. It is disturbing to note the development of the multitude of penicillin resistant strains of bacteria. This is becoming a very real problem in the treatment of staphylococcal diseases. It should make us more careful in studying the sensitivity of the particular streptococcus which we may be attacking with antibiotics, but even here there are peculiarities of growth of bacteria in relation to dosage of drug which are unsolved.

IV. Other Infections and Allergic Reactions

There are many cardiac conditions due to infections which are dignified with the diagnosis of particular types of heart disease, but which are only the cardiac reflection of a generalized process. It is true, nevertheless, that the heart involvement may well be the most important aspect of the infection.

The prevention of the primary infection will clearly prevent such types of heart disease. In our time we have seen diphtheritic heart disease practically disappear in the United States through immunization and therapy. Similarly, syphilitic heart disease can be overcome by appropriate public health, preventive, and therapeutic methods.

We need not concern ourselves with all the infectious agents which can affect the myocardium. It is quite proper, however, to note the reawakening of interest in the concept of "myocarditis" which was minimized so far as the term "chronic myocarditis" was concerned during the past twenty-five years when hypertensive and coronary artery etiologies took over this classification.

We now know, however, that a multitude of agents may injure the heart muscle. During the war, in addition to bacteria, the rickettsial bodies (as in typhus and scrub typhus) were shown to be serious myocardial enemies. Trichinosis has been reemphasized, but most important are the influences of the virus diseases, against which we have the weakest preventive and therapeutic defense. In this field lies the most important cause of hitherto unexplained diffuse myocarditis. Saphir in 1941 and 1942 (11) discussed the problems of the autopsy table in this group.

Influenza A, primary atypical pneumonia, mumps, poliomyelitis, and psittacosis are some of the etiologic factors. Complicating the situation are the obscure mechanisms of allergy following the administration of sulpha drugs, the thiocyanates, and arsphenamine.

Prevention of acute, of chronic, diffuse or isolated, myocarditis involves therefore the prevention of the virus and rickettsial diseases. Rivers (12) states that "with the exception of diseases in the psittacosis-lymphogranuloma and typhus-Rocky Mountain spotted fever groups, viral and rickettsial maladies of human beings do not respond to known chemotherapeutic agents and antibiotics." The exceptions noted are affected by penicillin and sulfonamides, while the rickettsial diseases are influenced by large, frequent, and early doses of para-aminobenzoic acid.

It is probably true, as asserted by Scherf and Boyd (13), that "only a few individuals completely and permanently escape small inflammatory foci in the myocardium (myocarditis)" due to the frequency of infections and the common participation of the myocardium in even mild infections. Sabathié (14) has presented evidence of this participation as a cause of benign, but often persistent, arrhythmias such as premature beats following infections.

We must also realize the potential danger of drug allergy, especially to the sulpha group, in a small category of preventable heart disease.

There is one other infection, tuberculosis, which has been considered of minor importance in heart disease but which now is of recognizably greater significance with the increasing evidence that it is the major factor in constrictive pericarditis (Pick's Disease).

Pathological study such as that reported by Sprague, Burch and White (15) in 1932 indicated that rheumatic fever was not the cause of constrictive pericarditis and that insidious tuberculosis was the most probable etiology. This has been difficult to prove. More recent studies, especially from England, weight the evidence heavily toward tuberculosis as the most frequent cause.

I bring this up because of the development of a possible specific therapy for tuberculosis, streptomycin. However, it has been noted that the coincidence of pulmonary and pericardial tuberculosis is rare, and the insidious nature and difficult diagnosis in many cases of chronic pericardial disease present problems in the ready use of this drug on a preventive basis.

V. Hypertension

In coming to a consideration of the prevention of hypertensive cardiovascular disease we move into the field of speculation. This is particularly unfortunate because it is probably the greatest cause of cardiac disability in the overall situation in this country. We know, for example, that the life insurance companies find a correlation between overweight and high blood pressure. Some assert that there is a condition of menopausal hypertension reversible by estrogen therapy. Certain causes of hypertension such as diabetes, renal infections, phaeochromocytoma, overdosage with desoxycortico-sterone, lead poisoning, toxemia of pregnancy, coarctation of the aorta, and hyperthyroidism are amenable to therapy before irreversible cardiac damage occurs. But all these are numerically insignificant in comparison with "essential" hypertension.

I will not consider the therapy of this condition, but it may be said that such treatment as is effective in maintaining a significantly low diastolic pressure will, to a great degree, prevent hypertensive heart disease. In our experience lumbo-dorsal sympathectomy has been the most successful treatment up to the present time.

It was reported in the paper a week ago (April 1948) that Drs. Stewart G. Wolf, Jr. and Hans Selye at the meeting of the American College of Physicians in San Francisco had announced their findings on the cause of hypertension. They emphasized the effects of worry, fear, and nervous collapse in raising blood pressure and thickening arterial walls. Dr. Wolf believes that hypertension may be "a costly hangover from primitive man, an old defense reaction to maintain normal body equilibrium". Instead of being tense and sitting on the edge of your seat in the face of a possible automobile accident he advised that one should relax and curl up. Dr. Selye emphasized the dangers of persistent worry, fear, and hate in fatiguing our protective hormonal system.

Last week a Boston lady in her eighties asked me if it was all right for her heart for her to keep up her daily swimming in the ocean through October, and to ride her bicycle. She went out walking every day last winter, the snowiest winter on record, and fell down on the ice four times. But, as she said "I never hurt myself because I always fall as if I were drunk". I am sure she is not hypertensive.

VI. Cor Pulmonale

It seems logical to consider hypertension of the lesser circulation directly after systemic hypertension. From increase in pressure in the pulmonary vessels there arises the strain upon the right heart known as cor pulmonale.

This pulmonary heart disease may be acute or chronic, primary or secondary. Acute cor pulmonale is essentially the insult to the right ventricle produced by sudden embolic occlusion of a major branch of the pulmonary artery. Repeated smaller emboli may in time cause chronic strain upon the right heart, or chronic cor pulmonale. Intrinsic disease of the smaller pulmonary vessels with pulmonary hypertension may rarely be the factor causing primary cor pulmonale. Such a condition is found in pulmonary endarteritis, congenital vascular aphasia, and probably in the Eisenmenger complex.

Many other causes may result in chronic right heart strain, notably emphysema and

pulmonary fibrosis, chronic pulmonary infection, kyphoscoliosis, pneumoconiosis, and pressure on the major lung vessels by aortic aneurysm or tumor.

Secondary cor pulmonale is due to transmission backward of increased pulmonary venous pressure into the pulmonary arterial circuit. The most common cause of right ventricular strain is failure of the left ventricle, but the greatest cause of isolated right heart strain is mitral stenosis.

From this brief account it may seem that many causes of pulmonary heart disease may be checked, but there are two in particular in which there is the opportunity of direct preventive action. I refer to the prevention of pulmonary embolism, and to the effects upon the pulmonary vessels of the increased volume of blood flow due to patent ductus arteriosus.

Pulmonary emboli almost always originate in the deep veins of the legs and the incidence of dangerous, or fatal, phlebothrombosis can be very much reduced by venous ligation and the anticoagulants. It is well to remember that in all patients, especially older ones, confined to bed, and certainly in all patients with congestive failure, the serious complicating factor may be the element of right heart strain, often associated with coronary insufficiency, introduced by multiple pulmonary infarcts. In rare instances the repeated bombardment of the lungs by emboli from a fibrillating right auricle may make a trial of restoration to normal rhythm by quinidine a justifiable risk to take.

Emphasis has recently been placed upon the necessity for ligation of patent ductus arteriosus in all individuals in whom the diagnosis is made early in life. Improvement in operating technique originated by Gross has made such ligations routine in our clinic. Its value in promoting growth and development of the child, in preventing the susceptibility to bacterial involvement of the ductus, and in forestalling left or total heart failure, is indication enough for the operation. However, there is another reason for early operation, namely, the prevention of the additional element of right heart strain which is not a predominant feature of patent ductus arteriosus unless there are secondary changes in the finer pulmonary vessels, which may arise from the abnormal increase in pulmonary blood flow. The burden of pulmonary arterial hypertension may then cause right heart failure by the mechanism of what Douglas and his associates (16) at the Mayo Clinic call a "systemic right ventricle", or a right ventricle bearing the load of the systemic arterial pressure. In rare cases, also, as Zuschlag (17) has recently pointed out, the formation of thrombi in a patent ductus may be the source of fatal pulmonary embolism in children and presents a further reason for ligation.

VII. Coronary Artery Disease

In the field of the prevention of coronary atherosclerosis we are perhaps even more baffled than in that of hypertension. It has recently been suggested by Dr. Carroll L. Birch (18) that the best way to live long was to spend one's youth in the temperate zone where degenerative diseases are common but infections of youth are well controlled, and the older years in the tropics where degenerative diseases are much less common, and infections, which attack youth preponderantly, are the major causes of death.

Many long term investigations have started to try to uncover the lethal factors in our daily lives. Dr. Ansel Keys' group, for example, at the University of Minnesota is studying diet, physical activity, worry, and tension in a group of volunteers between forty-five and fifty-four years of age. This may tell us about the value of exercise after the age of forty. At a recent meeting of the Chicago Heart Association the value of Walter Camp's daily dozen exercises in keeping President Wilson's cabinet in fit condition was questioned. It was stated that Walter Camp died at sixty-six, and the only one who refused to take the exercises, Josephus Daniels, died at eighty-seven.

We are at present studying a group of individuals who had coronary occlusions under the age of forty. This study includes anthropo-

metric analysis through cooperation with Professor Hooton's Department at Harvard, metabolic, chemical, dietary, blood viscosity, psychic, and other factors. In all such studies young investigators are needed, since older ones will probably die before the research is completed. Fortunately all these studies throughout the world are additive and will eventually uncover facts of great value.

Suppositions about prevention of coronary disease are hardly more than opinions, colored by the personal experience or bias of the observer. With this apology I will state my own conjecture. Individuals of long-lived ancestry who remain thin and physically active, whose metabolism is on the plus rather than the minus side of the normal range, who avoid prolonged periods of fatigue, and who are not malignantly ambitious, seem to live long.

Hufeland (19), the able scientific friend of Goethe and Schiller, is reported to have said that "there is no instance of longevity in a professed idler. The truth is that he who is occupied on subjects requiring thought, has not leisure to be intemperate"; and as Brunaud said "literary men have, in all climates and times, usually been long lived".

Last year I examined, at my own request, the oldest living Harvard graduate, now almost 103 years of age. He was in the Class of 1867. He told me that in college his wind was never good enough to permit him to be an athlete, and he told his athletic friends he would bury them all. This he has done. He is a thin, frail appearing individual, who has always smoked and used wine in moderation. His electrocardiogram is normal. He would not permit his blood pressure to be taken as he considered it an unpleasant ordeal. This man was a teacher. He retired in 1906. Like my grandfather he recognized the value of relaxation. My grandfather retired at 50 to conserve his health, and by virtue of having a successful business man as his son he lived for forty-five more years.

The prevention of coronary disease should begin at birth, and methods for this may someday be devised if we can discover the essential variables in susceptible individuals. I have never been convinced that worry and nervous strain were more than precipitating factors of "coronary attacks". What are called the stresses and strains of modern life are perhaps no more disturbing than the tensions of previous millennia, such as the caveman's struggle with sabre-toothed tigers, or the medieval terrors of famine and the Black Death. What really causes the apparent increase in coronary disease is that men didn't live long enough in former ages to acquire it in impressive numbers.

As a practical procedure we are now advising low cholesterol diets in families with a high coronary disease inheritance and giving small doses of thyroid extract, starting with $\frac{1}{4}$ grain a day, to individuals when the metabolism is in the minus range and the blood cholesterol high. At the moment the most encouraging lead in the coronary problem seems to be the attempt to explain the aberrations of cholesterol metabolism and deposition.

To me, the most enlightening recent contribution to this old question of the role of cholesterol has come from the work of Moreton (20) at the Tyree Memorial Laboratory for Research on Arteriosclerosis in Salt Lake City. Whereas there has been a dispute about the significance of blood cholesterol levels in relation to arterial deposits he has shown the importance of the physical properties of the plasma lipids through an extension of the work of Hueper. He says, "In a recent report from this laboratory we presented observations on the physical state and particle size of the plasma lipids in sustained hyperlipemia of metabolic and experimental origin. It was shown that the lipid particles in the plasma in these known causative conditions of atherosclerosis are so large as to be readily visible in the dark-field microscope and are readily separated to the top in a definite lipid layer by moderate centrifugation, in contrast to normal plasma, wherein most of the lipid is stabilized in colloidal particles too small to be seen by darkfield illumination and not separated even by relatively high-speed centrifugation. Pri-

marily, it was shown that the lipid particles (*chylomicrons*) appearing in normal plasma during alimentary hyperlipemia are also of large colloidal size, directly visible in the dark field and readily separated by centrifugation, and contain cholesterol, thus duplicating the coarse particulate distribution of lipids as found in sustained hyperlipemia. From these observations, coupled with clues from the characteristic histogenesis of the lesion, the theory was put forth that the cumulative effect of many fatty meals over a lifetime, by producing these transient showers of large lipid particles in the plasma, is the underlying cause of atherosclerosis in normal humans."

"It is apparent that those large lipid particles which pass with the lymph into the intima incite the foreign-body response which is a characteristic histological feature of the origin and development of atherosclerosis. Triglycerides and fatty acids are rapidly resorbed from the depositing mixed-lipid particles. Cholesterol, which is difficult to resorb and remove, remains and accumulates as the predominant residue in the slowly developing lesion. Lipid particles which contain larger percentages of cholesterol, as in sustained hyperlipemia (hypercholesterolemia), leave a greater residue and build up lesions more rapidly than lipid particles which contain smaller percentages of cholesterol (*i.e.* chylomicrons). When this residue of inert and difficult-to-resorb cholesterol is thus trapped between the high-pressure blood column on one side and the internal elastic membrane on the other, it is withheld and prevented from being dispatched to the liver (and possibly other sites), where theoretically it could be relatively easily degraded or eliminated by cells that are specialized in such metabolic functions. Thus, the accumulation of lipids in the arterial intima seems to be a local, mechanical problem, and unrelated to general body balance or over-all metabolism of these substances."

"In conclusion, present evidence indicates that the ingestion of fat-rich meals, by producing the temporary appearance of large lipid particles in the blood, causes the normal defense mechanisms of the intima to retain some of these particles and thus gradually and infinitesimally to build up the full picture of stenotic and occlusive arterial disease."

With new techniques such as the use of radioactive isotopes, and perhaps decholesterolizing agents, we can look forward to advances in our knowledge in this obscure field of vascular degeneration.

VIII. Miscellaneous

There is a group of conditions responsible for cardiovascular effects which requires brief mention.

(1) *Vitamine deficiency*, especially vitamine B, can produce severe heart failure with cardiac dilatation and is preventable as well as reversible.

(2) *Anemia* of high degree results in an increase in cardiac output, tachycardia, myocardial anoxia, and dilatation of the heart. It also is preventable in the types of anemia which respond to therapy. In treatment one must member the relative lack of value of digitalis and the great importance of transfusion with washed red cells rather than whole blood.

(3) *Thyrotoxicosis and hypothyroid heart disease* are clearly preventable and reversible. They are mentioned only to point to the importance of their early recognition.

(4) *Ecotopic rhythms*, especially auricular fibrillation, in otherwise normal hearts can result in heart failure and the restoration and maintenance of normal rhythm by quinidine presents a real possibility of prevention of cardiac failure.

(5) *Arteriovenous aneurysms*, chiefly traumatic, may result in heart failure from increased blood flow in the absence of the restraining capillary resistance. This presents a dramatic instance of reversible heart disease when the aneurysm is amenable to surgery, but it can also be considered as preventable if the fistula is obliterated in time. In this group also should be placed the hemangiomas of the lung which act as serious arteriovenous shunts and may be

cured by surgery. Recent investigation has shown a similar mechanism to exist in Paget's Disease with increased blood flow through the vascular channels in the bones. So far this is not preventable.

(6) *Cardiac neurosis.* Among the disabling types of cardiovascular disease appears cardiac neurosis. Quite properly the pattern of effort syndrome, or neurocirculatory asthenia, was classified in World War II among the psychiatric rather than the cardiac disorders, and as anxiety neurosis. Whether or not this is truly preventable remains to be seen. One way in which it can be kept below the incapacitating level is, of course, by the prevention of another war. There are great numbers of marginal individuals who can make moderately satisfactory social and economic adjustments to civilian life who become utterly useless to the armed services in wartime whether or not they are exposed to any enemy action. Prevention of such emotional crackups belongs in the field of eugenics and social philosophy. There is, however, another category of cardiac neurosis which is preventable, and that is the apprehension based either upon an uncomfortable or terrifying experience, such as a bout of paroxysmal tachycardia, or upon that most baleful word in diagnosis—the term "borderline". I have been impressed with the danger of ever transmitting to a patient the idea that he has "borderline" pathology in his heart. These patients are the victims of the electrocardiographer who, for example, always calls lowering of the T waves evidence of "coronary sclerosis", without realizing the multitude of other benign causes for such changes, or of the physician who overinterprets functional murmurs.

I spend much of my time in reassurance of the victims of electrocardiographic ineptitude. I, therefore, plead for a definiteness in diagnosis and, wherever possible, the statement to the patient that there is nothing wrong with the heart, in order to prevent the crippling fears engendered by the terms "questionable" or "borderline".

IX. Prevention of Cardiac Disability

While the prevention of heart disease is as yet limited in practical methods, the prevention of cardiac disability can often be attained by foresight or by early therapy. The following are some events susceptible to alteration:

(1) Infection.
(2) Obesity.
(3) Emotional crises.
(4) Exposure to cold.
(5) Overeating.
(6) Prolonged fatigue.
(7) Excessive and unusual physical effort.
(8) Alcoholic excesses.
(9) Sexual excesses.

It is not unusual to find at autopsy in old individuals a coronary circulation that has withered, a myocardium with areas of infarction and fibrosis and vessels occluded by chronic arteriosclerosis, and yet in the history there has been no angina pectoris nor recognizable episode of acute coronary thrombosis. Since no one in this audience can tell the state of his coronary intima tonight I believe that he should continue his physical activities at a constant level if free from symptoms. He should avoid the events I have just noted and, if fortunate, he may carry to a long deferred grave a reasonably sclerotic coronary system as a companion to his silent gall stones, his healed tuberculous glands, and his mild cirrhosis of the liver.

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Experiences with the Use of Heparin and Dicumarol in the Treatment of Coronary Thrombosis and Thrombo-Embolic Disease*

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CURRENTLY there are two drugs, heparin and dicumarol, which are being effectively used for anticoagulant therapy. The two preparations differ greatly in their properties and pharmacologic action, and neither is an ideal drug from the therapeutic standpoint.

Heparin, a physiologic substance which has its origin in the mast cells of Ehrlich, is usually obtained commercially from beef lung. It is rapid and effective in action, and there are few contra-indications to its use. Disadvantages of the drug are its expense and the necessity of giving the drug parenterally. The duration of action is relatively short. If the need should arise, prompt neutralization of its effect can be produced by protamine.

Dicumarol [3,3′-Methylene-bis-(4-hydroxycoumarin)] was initially isolated from spoiled sweet clover, but is now prepared synthetically. It is inexpensive and is given orally. The drug is slow in action, and, in most patients, an effective therapeutic level is not reached for 48 to 72 hours. The effect persists for several days. Several contra-indications to its use, such as blood dyscrasias, severe anemia, malnutrition, shock, and renal and hepatic diseases obviate its use in many patients who need this type of therapy. Another disadvantage of dicumarol is the lack of an effective method by which the prothrombin level may be rapidly restored to normal if hemorrhage occurs.

The use of heparin and dicumarol together is a distinct advantage in some patients, especially at the beginning of therapy. Both drugs must be used under rigid laboratory control, as either may be responsible for serious hemorrhagic complications. It is almost essential that a patient be hospitalized for therapy with either of these drugs.

CORONARY THROMBOSIS WITH MYOCARDIAL INFARCTION

Since December, 1946, we have participated in a controlled study sponsored by the American Heart Association to determine the value of dicumarol therapy in coronary occlusion with myocardial infarction. Rigid criteria were followed in the selection of patients for the therapeutic and control groups. Patients admitted to the hospital on odd days were treated, and those admitted on even days acted as controls. This method was possible only on certain groups of ward patients. A total of 34 patients was studied in these two groups. Eighteen patients were treated with dicumarol and sixteen acted as controls. The same laboratory studies, which included daily prothrombin times, were done on each group. In addition to these cases, there were many other patients with proved acute myocardial infarctions (private, semi-private or ward patients) who were hospitalized at the Pennsylvania Hospital during this same period. Many of these patients were treated with dicumarol at the discretion of their physician, and others received the usual conventional therapies. All of these patients have been included in the

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present study so that a total of 35 treated cases and 51 untreated cases is now available for analysis.

Method. Dicumarol therapy was instituted as soon as the diagnosis of myocardial infarction was established, unless an obvious contraindication was present. Daily prothrombin times were taken on all patients by use of the Link-Shapiro modification of Quick's technique.

Prothrombin times were measured in seconds rather than percentage of normal. A therapeutic level of 30 to 35 seconds (about 15% to 20% of normal) was attempted, with the use of a control of 13 to 15 seconds. A daily (single) dose of 300 mg. of dicumarol was given for two or three days (occasionally more) until the prothrombin time approached the desired level. The daily dose was then reduced to about 100 mg. Somewhat less than 100 mg. was the average daily dose. As a rule, dicumarol therapy was continued for about four weeks, and occasionally longer.

Data. The analysis of results in the treated and untreated is made on the basis of a six-weeks period after the diagnosis was established. A final analysis, which will include follow-up studies on all patients, will be made at a later date. Since a detailed analysis of such a small group of patients is of no statistical significance, only the factors of mortality, thrombo-embolic complications, gross hemorrhagic manifestations, and other complications have been considered.

The incidence of thrombo-embolic complications and the total mortality in the treated and control groups is shown in Table I. The cause of death other than thrombo-embolic complications is outlined in Table II. In Table III, the type of thrombo-embolic complications during the six-weeks study period is given for the treated and the untreated patients. Gross hemorrhagic complications were not seen in the untreated patients, but occurred twice in the treated group. One patient developed gingival bleeding, melena, and hematuria. In a second patient, hematemesis occurred and a psychosis developed which was considered as probably being related to cerebrovascular lesions. Both patients responded satisfactorily to large doses of Vitamin K and whole blood transfusions.

Obviously, in studying such a small group of patients, the results may do little more than indicate a definite trend. The large controlled series of patients being collected by a special committee of the American Heart Association will be analyzed in great detail. In a preliminary analysis of the first 800 cases, the results seem quite encouraging. The death rate in the control series was approximately 23%, but only 13% of the treated patients died. Thrombo-embolic complications occurred in 19% of the untreated, and in 9% of the treated patients. Hemorrhagic manifestations (any type) were seen in 3.7% of the control group and 11% of the treated group. Serious hemorrhagic complications were rare. In this large series, the two groups are quite comparable as to age, sex, severity, and recurrent attacks (6). The final report, which will include a detailed analysis of 1000 cases, is awaited with much interest.

TABLE I

THROMBO-EMBOLIC COMPLICATIONS AND MORTALITY RATE IN PATIENTS WITH MYOCARDIAL INFARCTION

(Six-Week Study Period)

	CONTROL (51)	TREATED (35)
1. Thrombo-embolic complications	12 (23.5%)	6 (17.1%)
2. Thrombo-embolic deaths	9 (17.6%)	2 (5.7%)
3. Deaths (other causes)	9 (17.6%)	1 (2.8%)
Total mortality rate	18 (35.3%)	3 (8.6%)

THROMBOPHLEBITIS AND PULMONARY EMBOLISM

The problem of thrombophlebitis, phlebothrombosis, and pulmonary embolism is an interrelated one and of great importance in the fields of both surgery and medicine. The work of Zilliacus, Allen, Barker, Jörpes, Murray, Wright, and others, leaves little doubt

as to the value of anticoagulant therapy in these conditions. The results of large series of patients with thrombophlebitis or phlebothrombosis treated by heparin, heparin and dicumarol, or dicumarol alone, are remarkably good. In the prevention of pulmonary embolism, the method seems as effective as surgical ligation. In untreated patients who have survived a pulmonary embolism and have been immediately heparinized, the final mortality rate is most significant. From one-fifth to nearly one-third of the untreated patients in this category die of later emboli which are usually multiple. The death rate has approached the zero level in the treated groups.

TABLE II

Causes of Death Other than Thrombo-Embolic Complications*

(Six-Week Study Period)

TYPE COMPLICATION	CONTROL (51)	TREATED (35)
1. Cardiac failure	4	0
2. Bronchial pneumonia	2	0
3. Ruptured heart	1	0
4. Ruptured I-V septum	1	0
5. Unexplained sudden death	1	1
Total	9 (17.6%)	1 (2.8%)

* In patients with myocardial infarction.

Coincident with the study on coronary thrombosis, we have been interested in studying patients of the medical, surgical, obstetrical and gynecological departments of the Pennsylvania Hospital on whom a diagnosis of thrombophlebitis, phlebothrombosis, and/or pulmonary embolism was made. All patients were seen by a member of the cardiovascular department and by a member of the surgical division, prior to instituting therapy of any type. An attempt was made to determine treatment best suited to the individual patient, and most of them were treated by anti-coagulant therapy or surgical ligation. In a smaller group of patients, no special therapy was given. Patients in whom surgical ligation or anticoagulant therapy was used prophylactically are not included in this series.

A total of 102 patients with thrombophlebitis or phlebothrombosis have been followed during a fifteen month period. We have been surprised at the high incidence of pulmonary embolism in this small series. It can also be assumed that a considerable number of patients had pulmonary emboli which were not recognized. Venograms were done on those

TABLE III

Thrombo-Embolic Complications in Patients with Myocardial Infarction

(Six Week Study Period)

TYPE COMPLICATION	CONTROL (51)		TREATED (35)	
	Cases	Deaths	Cases	Deaths
1. Pulmonary embolism				
A. Uncomplicated	2	2	6	2
B. With thrombophlebitis	2	1	0	0
C. With cerebral embolism	2	2	0	0
D. With renal infarct	1	1	0	0
E. With splenic infarct	1	1	0	0
2. Cerebral embolism	2	1	0	0
3. Thrombophlebitis	1	0	0	0
4. Mesenteric emboli	1	1	0	0
Total	12	9 (17.6%)	6	2 (5.7%)

Note: Death occurred in 75% of the control group with thrombo-embolic complications. This is in contrast to the 33.3% mortality in the treated group with thrombo-embolic complications.

patients in which the method was applicable. This was in approximately one-half of the cases, and it was found frequently to be of value in diagnosis and in determination of the degree of involvement. The types of treatment used in this group of 102 patients is summarized in Table IV.

Method. In nearly all of the medically treated patients, heparin therapy was begun as soon as the diagnosis was made. The intermittent intravenous method was utilized in nearly all instances. The coagulation time was first determined by the Lee-White method, and if this was within normal limits, 50 mg. of heparin were given. In four to five hours, the test was repeated, and if the clotting time had returned to normal, or nearly so, a regimen of 50 mg. of heparin every six hours was instituted. Frequent clotting times were not done in using this plan. On a few occasions, continuous intravenous heparin was used, and in these patients an attempt was made to keep the clotting time at three times the normal for that individual. Dicumarol was started at once in those patients in whom there were no contraindications, and in most of these heparin could be discontinued after two or three days. When the two drugs are used concomitantly, blood for the daily prothrombin time should never be taken immediately after a dose of intravenous heparin. The dosage of dicumarol was similar to that used in the myocardial infarction cases. Elastic bandages and immobilization were utilized in patients with acute thrombophlebitis in the early stages, but as soon as improvement was evident, early ambulation was stressed. It was seldom necessary to continue anticoagulant therapy more than ten to fourteen days in this type of patient.

TABLE IV

TYPES OF TREATMENT IN 102 CASES OF THROMBOPHLEBITIS AND PHLEBOTHROMBOSIS

TREATMENT	CASES TREATED
1. Anticoagulants (Heparin and Dicumarol)	49
2. Surgical ligation	30
3. Untreated:	
A. Undiagnosed	8
B. Other reasons	15
Total	102

TABLE V

THROMBOPHLEBITIS AND PHLEBOTHROMBOSIS: SUMMARY OF 49 CASES TREATED WITH ANTICOAGULANTS

CAUSE	TOTAL NUMBER OF CASES	CASES COMPLICATED C̄ PULMONARY EMBOLISM	EMBOLI AFTER TREATMENT	DEATH
Post-traumatic	5	1	0	0
Post-operative	16	4	1**	0
Post-infectious	4	1	0	0
Varicose veins c̄ or s̄ operations	2	0	0	0
Medical conditions*	19	11	0	1
Post-partum	3	1	0	0
Total	49	18	1	1

* Medical conditions were: Arteriosclerotic heart disease, cerebral embolism, rheumatic heart disease, acute myocardial infarction, diabetes mellitus, lobar pneumonia, and chronic cor pulmonale with multiple venous thrombosis.

** Occurred during the early course of heparin treatment.

Data. A detailed analysis of the symptoms and signs in the patients with thrombophlebitis, phlebothrombosis and pulmonary embolism is not within the province of this paper. The type of patient in which these conditions occurred was quite similar in the three therapeutic groups. Chronic medical diseases,

post-operative and post-partum cases made up the majority of the patients in all groups. In Tables V, VI, and VII, the complications before and after treatment and the mortality are summarized. The untreated cases represent a definitely weighted group as far as complications and mortality in the three therapeutic groups.

Discussion. In the past two decades, much progress has been made in increasing the accuracy of diagnosis of coronary thrombosis and myocardial infarction. A much broader

TABLE VI

THROMBOPHLEBITIS AND PHLEBOTHROMBOSIS: SUMMARY OF 30 CASES TREATED BY SURGICAL METHODS

CAUSE	TOTAL NO. OF CASES	CASES COMPLICATED C̄ PULMONARY EMBOLISM	EMBOLI AFTER TREATMENT	DEATH
Post-operative	7	4	2	2
Post-infectious	2	2	1	0
Varicose veins c̄ or s̄ operations	10	4	1	0
Post-partum	5	0	0	0
Medical conditions*	6	3	1	1**
Total	30	13	5	3

* Medical conditions were: Diabetes mellitus, rheumatic heart disease, generalized arteriosclerosis and heart disease, hypertensive cardiovascular disease, and Hodgkin's disease.

** Died of spinal metycaine anesthesia.

TABLE VII

THROMBOPHLEBITIS AND PHLEBOTHROMBOSIS
Summary of the 23 Untreated Cases

CAUSE	TOTAL NO. OF CASES	CASES COMPLICATED WITH PULMONARY EMBOLISM	DEATH
Post-operative	4	2	2
Post-infectious	1	0	0
Varicose veins c̄ or s̄ operations	4	2	1
Post-partum	3	0	0
Medical conditions*	11	8	6
Total	23	12	9

* Medical conditions were: Acute myocardial infarction, subacute bacterial endocarditis, diabetes mellitus, acute infectious hepatitis, and generalized arteriosclerosis.

TABLE VIII

THROMBOPHLEBITIS AND PHLEBOTHROMBOSIS
Summary of Results of All Types of Treatment

TYPE THERAPY	TOTAL CASES	SIMPLE VENOUS THROMBOSIS	CASES COMPLICATED C̄ PULMONARY EMBOLISM	EMBOLISM AFTER THERAPY	DEATH
Anticoagulant	49	31	18	1*	1
Surgical	30	17	13	5	3**
Untreated	23	11	12	0	9
Total	102	59	43	6	13

* Occurred early in the course of Heparin therapy.

** One patient died during spinal anesthesia.

mortality goes, because of the large number of undiagnosed patients, and the poor general condition of many of the others in this category. It does illustrate the high mortality rate in patients with thrombophlebitis and phlebothrombosis who receive no special therapy. Table VIII summarizes briefly the concept has been obtained regarding coronary disease, collateral circulation, and the myocardial changes which may follow gradual or rapid coronary occlusion. No major improvement in therapy has occurred during this period, however, and the incidence of complications and the mortality following myocardial infarction has changed little or none. The introduction of this new therapeutic principle would seem to offer distinct advantages over the previous treatments. There is little

doubt that widespread use of anticoagulant therapy will follow if it is proved to be efficacious. If more satisfactory anticoagulant drugs can be developed, which seems logical, the method may be applicable for use in non-hospitalized patients.

The good results reported in large series of patients with thrombophlebitis and phlebothrombosis by both anticoagulant and ligation therapy suggests that each method has merit. The treatment of a large number of consecutive patients by one method or the other has been of distinct scientific and statistical value. Contrary to the study of coronary thrombosis, the alternate case method is less applicable to this problem. It would seem, therefore, that we are rapidly approaching the time when criteria should be determined for the type of case best suited for surgical and for anticoagulant therapies. Probably the use of both methods in some patients is logical. The problem of pulmonary embolism is a more complicated one, but the value of anticoagulants in greatly lowering the mortality rate has been demonstrated by several investigators.

Summary

1. We have found dicumarol to be a safe drug in the therapy of patients who are hospitalized for coronary thrombosis with myocardial infarction.

2. Evidence is accumulating that anticoagulant therapy is effective in reducing the mortality and thrombo-embolic complications in patients with acute myocardial infarction.

3. Heparin and heparin plus dicumarol are effective therapeutic agents in the treatment of thrombophlebitis and phlebothrombosis. In selected cases, anticoagulant therapy may be as effective and perhaps more desirable than surgical ligation therapy.

4. In patients with pulmonary embolism with an obvious focus of origin, anticoagulant therapy with or without surgical ligation is indicated. With non-fatal pulmonary embolism from an unknown source, anticoagulant therapy should be started at once, and is the treatment of choice.

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The Iconography of Benjamin Rush*

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BEFORE the camera became a popular method of preserving for posterity the features of great and not so great, the chief means of portrayal was by the use of paint and brush. These were often later followed by the graver's tools for the purpose of wider dissemination. Sitting for a portrait was apt to be time consuming as well as expensive. As a result, old portraits, as compared to present day photographs, are comparatively rare. So it is that original reproductions of Benjamin Rush, one of the most famous Americans of his day and age, are actually not many in number. While most of them have been published far and wide, this is the first attempt, so far as I know, to gather them all in one basket. The limitations of this paper preclude the reproduction of them all, but three in particular are presented in the hope that they will elicit some desirable information. Figures 1 and 2, as we shall see, are doubtful portraits. I hope some time some one will clear up our doubts. Figure 3, as far as I know, has not been previously broadcast in any publication. It is a good likeness, if we make allowances for the ravages of time, and deserves to be presented for public use. Perhaps some one of our readers may even know who drew it.

The first of the originals that we know of was painted by Benjamin West while our own Benjamin was a medical student abroad. This was executed, no doubt, out of pure friendship, for it is unlikely that the impecunious American could have met that widely used portraitist's prices. It was done in 1769. After taking his degree in medicine at Edinburgh in 1768, Rush registered as a student in St. Thomas' Hospital and lived in London until February, 1769. During his stay in London he lived with the family of Benjamin Franklin. It was there he met Benjamin West, and the two remained firm friends, and corresponded with each other for many years afterwards. Numerous references exist which state that West entertained Dr. Rush while he was in London, and on one occasion gave a dinner which was also attended by Sir Joshua Reynolds, Dr. Samuel Johnson and Dr. Oliver Goldsmith.

A biographical sketch of Benjamin West in Scharff and Westcott's "History of Philadelphia" states that such a portrait was in possession of Dr. W. Kent Gilbert and that West painted Dr. Rush while he was a student in London. In 1887 at the centennial celebration of the College of Physicians of Philadelphia, a portrait of Dr. Benjamin Rush, loaned by Dr. A. W. Biddle, a descendant, was exhibited as a painting by Benjamin West. This portrait was presented to the College of Physicians by Mrs. Louis A. Biddle through Dr. O. H. Perry Pepper in May, 1943 (Fig. 1). There is a letter attached to the portrait, signed by Dr. Richard Henry Rush and addressed to Mrs. Biddle, which makes reference to a print, but so far no print has been found. Of late, some doubts have been cast as to the authenticity of this portrait, for it seems there are some who say this is not Benjamin Rush. It shows the still youthful doctor (he was only 23 at the time) with one hand resting upon a skull. This was a favorite symbol of the medical profession used by artists at this period and the same pose occurs in portraits of other doctors of this era.

The next portrait that I have (Fig. 2) is a photographic reproduction of what seems to be an oil painting. There are two copies of

* Presented before the Section on Medical History of the College of Physicians of Philadelphia, 29 March 1948.

this photograph in possession of the Historical Society of Pennsylvania, but sad to relate, no one there seems to know where they came from, or how. The name Rush is written on the back of each. As you see, Dr. Rush is pictured as a handsome youth, seated, with pen in hand, pausing as he writes, his left hand resting on his knee. Throughout his entire life he plied that pen vigorously. The picture is thus a very apt one, at least. It has been attributed to Charles Willson Peale. It does not resemble any other and time alone shall serve to unravel the mystery of its artist and provenance. As far as I know, neither of these portraits was known to his contemporaries, for I have never seen any other reproductions of either of them, while nearly all his other portraits have been repeatedly copied and recopied. This could, of course, be explained by the fact that at the age of 23 he was comparatively unknown, yet it is strange that of all his pictures, neither of these seems to have previously come to light.

FIG. 1. A PORTRAIT SUPPOSED TO BE OF BENJAMIN RUSH, AT THE AGE OF 23, AND TO HAVE BEEN PAINTED IN LONDON BY BENJAMIN WEST
(Original in possession of the College of Physicians of Philadelphia)

The next portrait of Rush was done in 1796 when he was 50 years of age by James Sharpless. James Sharpless was born in England

about 1751. He came to America in 1793 where the additional "s" was added to the spelling of his name. Although he painted in oil too, his successful practice in this country was in crayons, or pastels, which he manufactured himself and suited to the diminutive dimensions of his portraits which were generally in profile. These were usually finished in about two hours and priced at fifteen dollars. His wife, Ellen Sharpless, and his sons, Felix and James, Jr., were also skilled in this work and made many copies of their original drawings. In her diary, Mrs. Ellen Sharpless mentions that in May and June she commenced copies of Dr. Rush. One is now in possession of the Royal West of England Academy at Bristol, England. A beautiful pastel, six inches by nine inches, drawn by Sharpless can be seen at Independence Hall in Philadelphia. A head of Rush by the Sharplesses is also in Bristol, England. In addition to the pastels, one was done in pencil.

FIG. 2. A PORTRAIT SUPPOSED TO BE OF BENJAMIN RUSH. THE LOCATION OF THE ORIGINAL IS UNKNOWN. (Original photographs in possession of the Historical Society of Pennsylvania)

In all these portraits, the artist is said to have stuck to reality, producing a likeness which it was asserted any friend could recognize at a glance. A stipple engraving of the

Sharpless profile was published as the frontispiece of the June 13, 1797, number of the American Universal Magazine (Vol. 2) and L. H. Butterfield used it to form the frontispiece of his republication of Dr. Rush's letter on Franklin and Marshall College.

We next see Dr. Rush four years older in an oil portrait by Edward Savage. It gives a handsome, full faced view of the university professor at 54, in his prime, by now the most eminent physician in the new world. Of all the portraits, this one most nearly resembles figure 2 if we allow for a difference of over thirty years in age.

Edward Savage, the artist, was originally a goldsmith, a trade that produced many of our early American engravers. He studied under Benjamin West and painted portraits of several Revolutionary War notables. Savage also learned the art of engraving in stipple and in mezzotint and engraved the portrait of Rush, dating his engraving February 6, 1800. This was later reproduced on copper by L. E. Faber, a Philadelphia painter and etcher who died in 1913.

On the west wall of the Mütter Museum at the College of Physicians of Philadelphia there hangs a small colored mezzotint (or water color) portrait of Dr. Rush dated 1800 (Fig. 3). It is in a frame mounted with a picture of the University of Pennsylvania on Ninth Street, beneath. Little is known about this picture. In the Dreer collection at the Pennsylvania Historical Society there is a volume of "Letters of Benjamin Rush, M.D., 1793 to 1813" in which a portrait of Rush is present as the frontispiece. It is listed as an engraving but may actually be a lithographic reproduction. The most interesting thing about it, is, however, that it most nearly resembles the portrait in the Mütter Museum of the College of Physicians.

In 1802, when Rush was 56 years of age, a beautiful miniature portrait of him was drawn by St. Memin. A copy is in possession of the Historical Society of Pennsylvania and another, not signed, but quite evidently by the same artist, is at the American Philosophical Society, also dated 1802.

Charles Balthazar Julian Fevret De St. Memin, a French engraver, came to America after the French revolution. He perfected a device for reproducing the human face on copper with was then etched and finished in aquatint, resulting in a soft, pleasing print. These small portraits became very popular and St. Memin, traveling from North to South over the country produced about 800 of them. He made copies of most, some of which he signed and some he left unsigned, and a collection of these copies is now in the Corcoran Art Gallery at Washington, D. C. The Rush etching is also reproduced in a volume of "The St. Memin Collection of Portraits Consisting of 760 Medallion Portraits Photographed from Proof Impressions of the Original Copper Plates." It is *153 and appropriately enough rests alongside the profile of Thomas Parke, his fellow worker in the yellow fever epidemic of 1793.

In 1804 L. Lemet was located in Philadelphia. He produced an engraving of Dr. Rush which is now in the possession of the Pennsylvania Historical Society. Lemet was a close follower of the methods of St. Memin, producing portraits by the same means, and identical in appearance and size.

The same year, 1804, another portrait of Rush was drawn, this one by William Haines. The original drawing belonged to our revered friend, the late Dr. William Pepper and is on view at the library of the Medical School of the University of Pennsylvania. An engraving of this portrait by W. R. Jones is in the Edgar Fahs Smith collection at the University of Pennsylvania. I have a copy and have seen several others around. It was reproduced as the official portrait by the American Psychiatric Association at the centennial celebration. It does not make out Rush as fine looking as the Savage portrait, but apparently the doctor was aging fast after the age of 56. William Haines, the artist who drew this picture, was an excellent engraver of portraits in the stipple

manner, as was the American born William R. Jones, who reproduced it somewhere between 1810 and 1824 during the time he lived in Philadelphia.

done by Thomas Sully when Rush was about 65 years of age. As a matter of fact, Sully painted a number of portraits of the great doctor. The first one was done for Dr. Dewees.

Fig. 3. Small Colored Mezzotint (or Water Color) Portrait of Benjamin Rush; Artist not Known (Original in possession of the College of Physicians of Philadelphia)

Another portrait of Rush was done by Jeremiah Paul. This was then engraved by J. Akin. A copy is at the Historical Society of Pennsylvania. Then there is an oil portrait at Princeton by J. T. Vinar, a profile evidently done fairly late in life.

The most widely known and most frequently reproduced portrait of Benjamin Rush was

It was begun April 3, 1809 and finished May 21. Sully listed it as a bust and charged $50.00 for it. The second was done for Dr. Hosack, and it is the one with head resting on hand, seated and seen to his knees. Of this portrait, Dr. Samuel Jackson, who knew Rush well at the time, declared it was a perfect likeness. It is the one most often reproduced by Sully,

himself, and all the other copyists. Sully began to work on it May 7, 1812 and had it finally completed July 20.

Speaking of the several portraits he took of Rush, the artist said that the doctor never failed to be present at the appointed minute, for Rush was a most punctual man. The price of this painting was one hundred dollars. At the death of Rush, in 1813, Sully was commissioned to paint copies. The copy for the Pennsylvania Hospital, full length, seated, head resting on hand, glasses propped above his forehead (Rush had evidently not adopted bifocals, as did his friend, Benjamin Franklin), gray clothing and red curtain in the background, size 5′2″ x 6′ 11″, was noted in the artist's personal register as follows: "Deceased, painted from my first picture. Price $400.00." The engraving by David Edwin was from this copy.

Another copy was painted by Sully for Dr. Rush's daughter, a half length begun October 12, 1813, and finished in January, 1814. He also painted a copy in 1815 for the American Philosophical Society and even reproduced one as late as 1857, a bust only, for a Judge Black (or Blade?).

The original and copies of the Sully portrait have been reproduced in a great many places. John Neagle, a Philadelphia educated portrait painter born in 1796, is credited with the copy in oil done for the University of Pennsylvania; Richard B. Farley, of New Hope, Pa., a pupil of Whistler, made a copy for Dickinson College; Charles Willson Peale's copy hangs in Independence Hall; here, in our own College of Physicians there is a three quarter length copy by Adele Von Humbold, presented by Mary and Catherine Rush in 1888, and a miniature, which may even have been done by Sully, himself, for he did many miniatures. At Dickinson College there is one by Frederick Roscher; a copy is at the Pathology Department of the University of Pennsylvania; and there is even a copy on silk at the Ridgeway Library. Many excellent engravers were employed, also, to make copies for various purposes. William S. Leney, a fine Scotch engraver who settled in New York about 1805, made one from Dr. Hosack's portrait of Rush which was published in the American Philosophical Register of 1814 and in the Analectic Magazine the same year. Richard W. Dodson, an engraver of portraits and book illustrations, reproduced the portrait in possession of Richard Rush, Esquire, for publication in Longacre's National Portrait Gallery of 1836. It was republished in 1853, 1865 and in 1896, the last in Fiske's American Review. Dr. William Pepper used this engraving in his rare book on the "Medical Side of Franklin", a book that has really become a collector's item. David Edwin, who settled in Philadelphia in 1797, and for thirty years was the most prolific engraver of portraits in America, made a copy from the Pennsylvania Hospital portrait which was published along with a eulogy of Dr. Rush in Delaplaine's Repository in 1813, in the Portfolio the same year, in Timothy Alden's "Collection of American Epitaphs" (1814), in Museum for Literature and Science (1826), Thacher's "American Medical Biography" (1828), in Casket (1829). Christian Gobrecht, a Pennsylvania Dutchman made an engraving which was published by Samuel C. Atkinson of Philadelphia; J. W. Orr of New York engraved a copy for the American Portrait Gallery (1838) which was reproduced in Jones' illustrated American Biography in 1853; a nice mezzotint was engraved by Gross for Simpson's "Eminent Philadelphians" (1859) which was used by Samuel D. Gross in his "Lives of Eminent Physicians"; a lithographic reproduction was made by James B. Longacre and can be seen in the College of Physicians of Philadelphia. Sanderson used it in his "Biography of the Signers of the Declaration of Independence" published in 1823. Another lithograph was done by Albert Newsam, an interesting American artist who was born deaf and dumb at Steubenville, Ohio, in 1809 and studied art under George Catlin. This Rush picture is not included in Stauffer's list of Newsam's Works, which does include other Philadelphia

physicians (Robert M. Bird, John Godman, etc).

Finally there are numerous reproductions of various types in such places as Thomas George Morton's History of the Pennsylvania Hospital, Nathan Goodman's biography of Benjamin Rush, Harper's Magazine for 1876, Duncan's Medical Men of the American Revolution and Duyckinck's Cyclopedia of American Literature; Edwin Austin Abbey's "Apotheosis" in the House of Representatives at Harrisburg, Pa., John Trumbull's oil painting of the Signers of the Declaration of Independence; a sketch at the John Wanamaker Store in Philadelphia showing "Dr. Benjamin Rush aiding sufferers in the yellow fever plague in 1793".

The final likeness which I shall mention is a silhouette in the Wm. M. Coates collection of the Pennsylvania Historical Society, showing Rush with a wig with long plait and ribbon and ruffled collar, and a youthful profile. We, too, have a silhouette here at the College of Physicians and there is another in the Miller collection at the Academy of Medicine in Richmond, Va. Not any of these three bear any resemblance to each other. Perhaps the artists differed in their reproductions. Perhaps the deviations from each other are to be accounted for in the different appearance of the subject at the different ages at which these were done.

Silhouettes derive their name from that of a Frenchman, Etienne de Silhouette who developed and popularized the art while in exile in London. While he did some 4,000 American portraits, it was Charles Willson Peale and William H. Brown who produced the best and most notable American examples. The Rush silhouette in the Miller collection of the Richmond Academy of Medicine was done by our own Charles Willson Peale. For a delightful account of these "shadows of the medical past" turn to the January 1938 issue of the Bulletin of the Medical Library Association and read the glowing account of "A Collection of Medical Silhouettes" by that genial West Virginia antiquarian, Joseph Lyon Miller.

Besides the portraiture of Benjamin Rush, a fine bust was made of him by his cousin, an ingenious wood-carver, William Rush and a number of replicas are scattered in different institutions with which Dr. Rush was connected in Philadelphia. There are also a number of medals listed, one of which was made in 1808 by M. Furst while he was working at the U. S. Mint. A complete list of books, journals, articles, papers, etc., in which pictures of Rush are reproduced would be an utterly impossible task to undertake. The best reference source that I know of, and the one upon which this entire study is based is the Wm. N. Bradley collection. This is a comprehensive collection of portraits of Philadelphia physicians assiduously gathered and nurtured with that loving care of a collector known only to the initiated. Through the generosity of the owner it is now housed in the College of Physicians of Philadelphia for the common use of all.

Memoir of Samuel Bradbury*

By WILLIAM D. STROUD

DR. SAMUEL BRADBURY was born in Germantown, Philadelphia, on April 30, 1883 and died on August 30, 1947 with pneumonia complicating an acute coronary occlusion which occurred while vacationing in Maine.

Dr. Bradbury attended the Germantown Friends School and graduated from the University of Pennsylvania Medical School in 1905. After an internship at the Germantown Hospital and six months at the Lying-In Hospital, New York, he spent two years as intern and two years as Chief Resident at the Pennsylvania Hospital. He began the practice of medicine in New York City in 1912 and during this time was Visiting Physician at the City and Bellevue Hospitals, Instructor in Medicine at Columbia University 1912-1921 and Chief of Clinic and Assistant Professor of Clinical Medicine at Cornell University Medical College.

In 1914 he married the former Althea Norris Johnson of New Orleans and Mrs. Bradbury and their two sons and two daughters survive him.

Dr. Bradbury was a veteran of the First World War, serving nearly two years in France and returning to New York in 1919. He returned to Philadelphia in 1927 and organized the Out Patient Department of the Pennsylvania Hospital and has been its Medical Director since then. He was also Director of the Medical Service of the Germantown Hospital from 1930 until the time of his death.

On May 6, 1929 Dr. Bradbury was elected a Fellow of the College and he has always taken an active interest in its affairs. He was a member of the American Medical Association, Medical Society of the State of Pennsylvania, Philadelphia County Medical Society, Philadelphia College of Physicians, Academy of Medicine of New York, American Clinical and Climatological Association, American Association for the Advancement of Science and the Harvey Society. He was Chairman of the Committee of Group Practice of the Medical Administration Service, a member of the Committee on Nursing Activity, Philadelphia Chapter of the American Red Cross; member of the Board of the Family Society of Philadelphia and of the Advisory Committee of the Group Health Association of Washington, D. C.

Dr. Bradbury was the author of "The Cost of Adequate Medical Care", "What Constitutes Adequate Medical Service" and coauthor of "Internal Medicine" in three volumes, as well as a contributor to the "Cyclopedia of Medicine" and to Cecil's "Textbook on Medicine".

All who knew Sam Bradbury were devoted to him. He was a fine Christian character who inspired confidence and a good friend, beloved by his patients and immensely admired throughout the Medical Profession. In his wide vision, he was keenly interested in and constantly looking toward the future of Medicine. He had the ability to push through innumerable tasks, however many came his way. He will be greatly missed by the hospitals with which he was associated and by his patients and friends.

* Read at the meeting of the College of Physicians of Philadelphia, 7 April 1948.

Transactions of the Sections

SECTION ON GENERAL MEDICINE

26 January 1948

Gastro - intestinal Allergy: Roentgenographic Demonstration and Treatment with Propeptans. Alison H. Price*, M.D., Edward J. Tallant*, M.D., and Frederick Urbach*, M.D. (*Abstract 1, below.*)

Needle Biopsy of the Liver: Technique and Diagnostic Application. Edwin A. Rasberry, M.D., and Winston K. Shorey, M.D. (*Abstract 2, below.*)

Emotional Factors in Gastro - intestinal Tract Disease. Stewart Wolf*, M.D.

23 February 1948

The Effect of Vomiting Due to Intestinal Obstruction and Other Causes on the Serum Potassium. Samuel Bellet, M.D., Carl S. Nadler*, M.D., and Mary Lanning*, A.B. (*Abstract 3, below.*)

A Consideration of Some Similarities and Differences between Infectious Mononucleosis and Infectious Hepatitis. J. Edward Berk, M.D., Harry Shay, M.D., and Joseph A. Ritter, M.D. (*Abstract 4, below.*)

Hemoglobinuria and Blood Destruction Resulting from Severe Thermal Burns. Thomas Hale Ham*, M.D.

22 March 1948

Massive Pulmonary Infarction in Periarteritis Nodosa. Samuel J. Goldberg, M.D., David R. Meranze, M.D., and I. Finestone*, M.D. (*Abstract 5, below.*)

Pneumonia at the Philadelphia General Hospital, 1936–1948. Harold L. Israel*, M.D., Robert C. Mitterling*, M.D., and Harrison F. Flippin, M.D. (*Abstract 6, below.*)

Fungus Diseases of the Lungs. Wiley D. Forbus*, M.D.

* *By invitation.*

26 April 1948[1]

Extreme Bradycardia. Joseph C. Doane, M.D., and Sidney O. Krasnoff*, M.D. (*Abstract 7, below.*)

Experiences with the Use of Heparin and Dicumarol in the Treatment of Coronary Thrombosis and Thrombo-Embolic Disease. Joseph B. Vander Veer, M.D., David S. Marshall, II*, M.D., and P. T. Kuo, M.D. (*Printed in full in this issue of the* Transactions and Studies.)

The Prevention of Heart Disease and Disability. Howard B. Sprague*, M.D. (*Printed in full in this issue of the* Transactions & Studies.)

24 May 1948

Hodgkin's Disease of the Stomach. Harold L. Goldburgh, M.D., Samuel Baer*, M.D., and Roscoe Teahan*, M.D.

The Blood Flow, Vascular Resistance, and Oxygen Consumption of the Brain in Essential Hypertension. Seymour S. Kety*, M.D., William A. Jeffers, M.D., Joseph H. Hafkenschiel*, M.D., Irving H. Leopold, M.D., and Henry A. Shenkin*, M.D.

The Use of BCG with Streptomycin in the Treatment of Tuberculosis: a Preliminary Report. F. Maurice McPhedran, M.D.

The Electrolytic and Electrocardiographic Changes during and following Therapy in Diabetic Acidosis, with Special Reference to Alterations in Serum Potassium and the Significance of These Changes in Treatment. Samuel Bellet, M.D., Carl S. Nadler*, M.D., and Mary Lanning*, A.B.

SECTION ON MEDICAL HISTORY

29 March 1948

The Iconography of Benjamin Rush.

[1] Joint meeting with the Philadelphia Heart Association.

Samuel X. Radbill, M.D. (*Printed in this issue of the* TRANSACTIONS & STUDIES.)

THE HISTORY OF MEDICAL RESEARCH IN THE UNITED STATES. Richard H. Shryock*, PH.D.

MEDICINE AND THE CHANGING ORDER. Iago Galdston*, M.D.

SECTION ON OPHTHALMOLOGY[2]

22 January 1948

OPHTHALMOSCOPIC SIGNS FOR AND AGAINST OPERATION TO RELIEVE VASCULAR HYPERTENSION. Arthur J. Bedell*, M.D.

19 February 1948

LAURENCE-MOON-BIEDL SYNDROME. O. A. Capriotti*, M.D.

OPHTHALMOLOGICAL RESEARCH FOR THE IMPROVEMENT OF FLUOROSCOPIC X-RAY SCREENS. Robert H. Peckham*, PH.D.

A GENETIC STUDY OF THE MARFAN SYNDROME. Frank C. Lutman*, M.D.

SUBZYGOMATIC DECOMPRESSION FOR EXOPHTHALMOS OF CRANIAL STENOSIS. Edmund B. Spaeth, M.D.

18 March 1948

INDICATIONS AND RESULTS IN KERATOPLASTY. Harold Scheie, M.D.

SOME OBSERVATIONS ON MIOTICS. Edwin B. Dunphy*, M.D.

22 April 1948

HETEROPLASTIC GRAFTS. O. A. Capriotti*, M.D., and Edmund B. Spaeth, M.D.

FOLLOW-UP STUDIES IN FIVE CASES OF INTRAOCULAR NON-MAGNETIC FOREIGN BODIES. James S. Shipman, M.D.

CORRELATION OF CEREBRO-VASCULAR RESISTANCE AND RETINAL VASCULAR FINDINGS. Irving H. Leopold, M.D., Seymour Kety*, M.D., William A. Jeffers, M.D., Joseph Hafkenschiel*, M.D., and Henry A. Shenkin, M.D.

[2] The presentations at this Section are customarily abstracted in the *American Journal of Ophthalmology* and the *Archives of Ophthalmology*.

SECTION ON OTOLARYNGOLOGY[3]

21 January 1948

MENACE OF THE DEVITALIZED TOOTH IN OTOLARYNGOLOGY. Howell B. Peacock*, M.D.

RHINOPLASTY (WITH ILLUSTRATIONS). Romeo A. Luongo, M.D.

CARCINOMA OF THE NASOPHARYNX: REPORT OF A CASE. Louis E. Silcox, M.D.

USE OF STREPTOMYCIN IN PHARYNGEAL ABSCESS: REPORT OF A CASE. Richard W. Rooker*, M.D.

18 February 1948

RHINOSCLEROMA. F. Johnson Putney, M.D.

METASTATIC ADENOCARCINOMA OF THE LARYNX. James T. Spencer, jr.*, M.D.

LARYNGEAL STENOSIS COMPLICATING IRRADIATION FOR THYROTOXICOSIS. Robert M. Lukens, M.D.

BROKEN NEEDLE IN TONSILLAR FOSSA: ATTEMPTED REMOVAL. William J. Hitschler, M.D.

DEMONSTRATION OF AN INSTRUMENT TO TEST SPEECH HEARING AND EFFICIENCY OF HEARING AIDS. Douglas Macfarlan, M.D.

17 March 1948[4]

THE DIAGNOSIS AND TREATMENT OF MÉNIÈRE'S DISEASE. Karl M. Houser, M.D.

THE SURGICAL TREATMENT OF CHRONIC DACRYOCYSTITIS. Kelvin A. Kasper, M.D.

RESULTS OF SURGICAL TREATMENT OF CANCER OF LARYNX BY THYROTOMY APPROACH. Gabriel Tucker, M.D.

21 April 1948

ANALYSIS OF RESULTS OBTAINED BY THE LABYRINTH FENESTRATION OPERATION OF 100 CASES OF OTOSCLEROSIS. Edward H. Campbell, M.D.

THE DIAGNOSIS AND TREATMENT OF ACUTE

[3] The presentations at this Section are customarily abstracted in the *Archives of Otolaryngology*.

[4] Joint meeting with the Section on Otolaryngology of the New York Academy of Medicine.

Infections of the Epiglottis. Joseph P. Atkins, M.D.

An Experimental Study of the Toxic Effects of Streptomycin on the Vestibular Apparatus of Cats. Part 1. The Central Nervous System. (A Preliminary Report.) Julius Winston, M.D., F. H. Lewey*, M.D., André Parenteau*, M.D., Philip A. Marden, M.D., and Faith Cramer*, M.D.

SECTION ON PUBLIC HEALTH, PREVENTIVE AND INDUSTRIAL MEDICINE

9 February 1948

The Importance of Good Reporting in a Communicable Disease Program. A. M. Perri*, M.D.

The Shifting Incidence of Diphtheria. A. C. La Boccetta, M.D.

The Part of a Virus Diagnostic Laboratory in Public Health. Thomas F. McNair Scott, M.D.

17 May 1948

The Present Problems of Maternal Welfare in Philadelphia. J. Marsh Alesbury*, M.D.

The Distribution of Child Health Services in the United States. John Mitchell, M.D.

Abstracts

Abstract 1

Gastro - intestinal Allergy: Roentgenographic Demonstration and Treatment with Propeptans. Alison H. Price, M.D., Edward J. Tallant, M.D., and Frederick Urbach, M.D.

The effects of specific foods upon the gastrointestinal tract were investigated in three types of patients: (1) patients with food hypersensitivity and gastrointestinal symptoms; (2) patients with food hypersensitivity without gastrointestinal symptoms, and (3) patients with no known food hypersensitivity.

After elimination of the suspected food from the diet for five days, roentgenograms of the gastrointestinal tract were taken at one, two, three, and six hours, using U.S.P. barium sulfate in water. Five days later the study was repeated, adding the suspected food to the barium sulfate in water. The patients with food hypersensitivity and gastrointestinal symptoms showed narrowing, segmentation and scattering of the barium in the ileum with occasional hypermotility when the allergen was given. There were no changes in the roentgenograms when the allergen was not given. There were no abnormal changes in the roentgenograms of the food hypersensitive patients without gastrointestinal manifestations or the patients with no known food hypersensitivity either with or without the allergen in the contrast medium.

The patients with food hypersensitivity and gastrointestinal symptoms were treated with type specific Propeptans. The symptoms were relieved in seven of the ten patients treated and the roentgenograms of all the patients were normal after treatment and no longer showed any changes when the allergen was given. The three patients in whom the symptoms persisted also had severe neuroses.

Abstract 2

Needle Biopsy of the Liver: Technique and Diagnostic Application. Edwin A. Rasberry, M.D., and Winston K. Shorey, M.D.

Lucatello in 1895 first aspirated material from the liver for diagnostic purposes. Bingel in 1923 and Olivet in 1926 revived the maneuver. Iverson, Roholm and Karump in 1939 popularized the procedure using a larger calibre needle and studying the tissue, after appropriate fixing and staining, like any other biopsy specimen. Baron first did needle biopsies of the liver in the United States in 1939.

The technique that we have used is that described by Jones and Volwiler. It involves

the use, under local anesthesia, of a needle with three sharp cutting teeth (Franseen modification of Iverson-Roholm instrument) that cuts out a small cylindrical section of liver tissue as it is being introduced. A stylet is kept in place until the needle reaches the liver and is then removed. After the hollow needle has been advanced with a rotary motion within the liver substance, a syringe is fitted to the needle and suction is applied. As the syringe and needle are withdrawn, the suction is maintained and the biopsy specimen slides into the syringe. The entire procedure is accomplished within 10 seconds, thus making it possible for the subject to hold his breath during the entire time. In this way a tear of the liver by its movement against the fixed needle is avoided.

To date we have attempted needle liver biopsy 85 times in 79 patients with no deaths. We have failed to get satisfactory tissue in two instances. The only complications have been excessive right upper quadrant pain, longer than 24 hours, in one patient and a pleural friction rub with a small pleural effusion in another.

CASE REPORTS

The following cases are presented as representative of those in which liver biopsy can be helpful in making a diagnosis.

J. D., a 24 year old white female, had a clinical diagnosis of infectious hepatitis. The liver biopsy confirmed this.

B. W., a 47 year old white male, had had infectious hepatitis four months before biopsy. Although he looked and felt well, his liver was still enlarged and there was a persistent retention of bromsulfalein. The microscopic diagnosis from liver biopsy was subsiding viral hepatitis.

C. S., a 65 year old white female, was admitted because of right upper quadrant pain, jaundice and weight loss. The diagnosis was not clear on clinical grounds. The biopsy sections revealed a great amount of bile in the canaliculi and pericholangitis compatable with an extrahepatic obstruction. At operation she was found to have carcinoma of the head of the pancreas.

J. R., a 45 year old white male, a chronic alcoholic, was clinically diagnosed as cirrhosis of the liver. The liver biopsy was confirmatory.

G. T., a 45 year old white male, who had been previously admitted on two occasions for alcoholic psychosis was found to have hepatomegaly, ankle edema and anorexia. Various laboratory tests gave conflicting evidence. By liver biopsy a diagnosis of cirrhosis of the liver was made.

T. L., a 30 year old white female, was admitted because of jaundice, hepatomegaly and weight loss. A T-tube was already in place from a previous choledochostomy. The diagnosis was not clear from clinical and laboratory findings. Section from the biopsy revealed biliary cirrhosis.

F. K., a 58 year old white male, was admitted because of epigastric pain, hepatomegaly and weight loss. The diagnosis could not be established from clinical, roentgenological or laboratory studies. Metastatic carcinoma of unknown origin was found in the biopsy section.

M. H., a 47 year old white female, was admitted in liver failure, the cause of which could not be found. By liver biopsy a diagnosis of hemochromatosis was made.

R. A., a 39 year old colored female, was admitted with fever of 103°F., tachycardia, pleural effusion, ascites, hepatomegaly and ankle edema. The diagnosis was not established on clinical or laboratory findings. The section from liver biopsy revealed many small tubercles scattered through the liver tissue consistent with a diagnosis of tuberculosis or Boeck's sarcoid of the liver.

There are other conditions in which liver biopsies have been of aid in diagnosis. They have also been helpful in watching the progress of certain diseases.

Objections to the procedure are the danger of hemorrhage, failure to obtain an adequate specimen in a small percentage of cases and the chance of not securing a specimen from

the involved area in spotty diseases of the liver. However, careful technique combined with proper selection and supervision of patients makes these objections minimal.

Abstract 3

THE EFFECT OF VOMITING DUE TO INTESTINAL OBSTRUCTION AND OTHER CAUSES ON THE SERUM POTASSIUM. Samuel Bellet, M.D., Carl S. Nadler, M.D. and Mary Lanning, A.B.

Until recently the alkalosis accompanying vomiting was commonly regarded as involving almost exclusively the balance of sodium and chloride in extracellular fluids and little significance was attached to the incidental changes in the ionic constitution of the cells themselves. Recently, the work of Butler, Fenn, Darrow, Talbot, Gamble and others have called attention to the alterations in the intracellular as well as extracellular fluid, which occur during alkalosis and acidosis with accompanying loss of fluids from the body. It has also been shown that sodium may pass from the extracellular fluid into the cell and replace potassium.

Scudder, in a series of 20 untreated cases of intestinal obstruction, found the serum potassium to be raised in 7, low in 5, and normal in 8. Falconer was unable to verify that hyperpotassemia was a factor in the intoxication of intestinal obstruction. He found that there was a diminution in the serum potassium before any treatment was begun, and during the period of treatment he observed a progressive decrease in concentration.

The object of this presentation is to report our experience with the electrolyte changes, particularly as they concern potassium in 15 cases associated with acute intestinal obstruction. Five of these were studied before any therapy was instituted and 10 soon after treatment in the form of parenteral fluids was started.

Our procedure in the study of these cases was as follows: Following examination, blood estimations were made including the hematocrit, total base and of the CO_2 and chlorides. These examinations were repeated at frequent intervals during the patient's course in the hospital. Electrocardiograms were taken simultaneously with the blood sample. Electrocardiographic studies were made and this study was initiated because we have observed for many years that electrocardiographic changes occur in patients with intestinal obstruction which we believed was the result of disturbances in the electrolytes. We shall show that these changes are due chiefly to a diminution in the serum potassium. The electrocardiogram was of inestimable value in two respects: a) in making a diagnosis of potassium deficiency; and b) in following the subsequent changes in the serum potassium values which can be fairly well shown by the electrocardiographic changes.

We found that the serum potassium in these changes was low on admission, the concentration ranging from 8 to 15 mgm. per cent. These concentrations became still lower following parenteral therapy with saline and glucose. These patients received intravenous injections of potassium in the form of a one and two-tenths per cent solution, and the effect of the injection upon the electrocardiogram and the serum potassium was noted. The amount administered ranged from 100 to 700 cc. given over a period of one to three hours. The low serum potassium tended to return to normal following the administration of potassium or the taking of food by mouth.

While it is felt that the alterations in other electrolytes may contribute to the general asthenic condition of the patient, it is felt that the low potassium contributes much to this state. Following the administration of potassium, there usually results an increase in blood pressure, improvement in the clinical state of the patient and improvement in the electrolyte picture of the other ions. The electrocardiogram parallels fairly well the serum potassium level and is of value not only in the diagnosis of hypopotassemia but in following the effects of therapy. The electrocardiographic changes due to a low potas-

sium are immediately reversible by the administration of potassium.

A significant lowering of the potassium level if maintained for any period of time is associated with disturbances of various body functions including the muscular nervous system and metabolic functions.

It is recommended that patients with low potassium be given potassium in addition to the other forms of parenteral therapy. This will not only aid in the patient's recovery but at times may be life saving.

We believe that the toxicity of potassium has been somewhat over-emphasized. Normal individuals with normal kidney function can be given fairly large doses by mouth (5 to 15 gms.) and parenterally up to 500 cc. in two hours, without untoward effects. To patients with hypopotassemia we have given not only these doses by mouth but 700 cc. of 1.2% intravenously and 500 cc. per day to supplement the electrolyte imbalance.

Abstract 4

A Consideration of Some Similarities and Differences between Infectious Mononucleosis and Infectious Hepatitis. J. Edward Berk, M.D., Harry Shay, M.D. and Joseph A. Ritter, M.D.

Infectious mononucleosis and infectious hepatitis may sometimes be difficult to differentiate from each other because of the common occurrence of hepatitis in the former and because of certain clinical and hematological similarities between them. The studies herein reported were undertaken in an attempt to determine other similarities or differences between these two disorders. The titer of heterophile antibodies in 25 patients with infectious hepatitis observed at varying periods after the onset of the disease indicated that high titers must occur only occasionally. No titer was observed in this group above 1:56 and only 3 of the 127 determinations were of this magnitude. Furthermore, contrary to infectious mononucleosis, boiled guinea pig kidney and boiled beef erythrocytes completely absorbed these antibodies in infectious hepatitis. In 12 patients with infectious mononucleosis the flocculation tests (thymol turbidity, 18 hour turbidity ratio, cephalin cholesterol flocculation, and colloidal gold), just as in infectious hepatitis, showed a remarkable tendency to be positive and to remain so long after the onset of the disease. On the other hand, the ratio of esterified to total cholesterol and sulfobromphthalein retention revealed abnormalities in only a small percentage of the cases of infectious mononucleosis. This discrepancy between the flocculation tests on the one hand and the tests accepted as measuring some function of the liver on the other, raises a question as to the significance of abnormal flocculation phenomena in infectious mononucleosis. Serum alkaline phosphatase tended to be elevated above normal during the first month of the disease in infectious mononucleosis just as in infectious hepatitis. However, elevations, sometimes quite pronounced, were observed in infectious mononucleosis even in those patients without jaundice.

Abstract 5

Massive Pulmonary Infarction in Polyarteritis Nodosa. Samuel J. Goldburgh, M.D., David R. Meranze, M.D., and I. Finestone, M.D.

The authors report a case of polyarteritis nodosa in a 39 year old woman, who had suffered from intractable asthma for 8 years. The illness terminated fatally, after 5 months. Clinical features consisted of exacerbation of asthma and of allergic nasal symptoms, severe peripheral neuritis affecting all four extremities, abdominal pain with nausea and vomiting and marked eosinophilia.

The immediate cause of death was respiratory insufficiency and anoxia resulting from massive bilateral infarction of both lungs, which occurred without prodromal symptoms, during a partial remission of the systemic disease. Lesions typical of periarteritis nodosa, with or without infarction were found

in the lungs, heart, kidneys, spleen, subcutaneous tissues, mesenteric vessels, pancreas and peripheral nerves. A large mural thrombus had formed on the lateral wall of the right ventricle and extended into the pulmonary artery and all its major branches. The thrombus was partially organized and almost completely occluded the blood flow to the lungs.

The diagnosis was made clinically and verified during life by biopsy of a subcutaneous nodule. Attention is called to the frequent association of the disease with asthma, and support is given to the concept that the necrotizing arteritis is a destructive manifestation of severe and irreversible allergy.

Abstract 6

Pneumonia at the Philadelphia General Hospital, 1936–1948. Harold L. Israel, M.D., Robert C. Mitterling, M.D., and Harrison F. Flippin, M.D.

A study has been made of lobar pneumonia at the Philadelphia General Hospital in 1936–37, a year in which specific therapy was not employed, in 1940–41, a year in which sulfonamides were generally applied, and in 1945–46, a year in which penicillin was available as an adjuvant to the sulfonamides. The case mortality rates were 23.3 per cent, 5.4 per cent and 6.5 per cent for the three years, the apparent slight increase in the last year being due to a striking rise in age of the patients.

Although the mortality of lobar pneumonia did not vary significantly between 1940–41 and 1945–46, highly significant differences between these years were observed in two respects: a reduction in white-cell counts on admission and a retarded temperature response to specific therapy. Detailed analysis indicates that these changes cannot be attributed to erroneous inclusion in the 1945–46 series of large numbers of viroid pneumonias.

A preliminary analysis of 128 patients studied in 1947–48 demonstrated the same reduction in admission white-cell counts, but there was no retardation of temperature response to therapy.

It is concluded that lobar pneumonia as observed in 1945–46 and 1947–48 had altered significantly from the disease encountered in previous years and in such fashion that it was clinically difficult to distinguish from viroid pneumonias. It is suggested that lobar pneumonia may represent an underlying viral process modified by superimposed bacterial infection. On this hypothesis, the temporal and geographic variations in lobar pneumonia may be due to differences in the viral or bacterial factors.

Abstract 7

Extreme Bradycardia. Joseph C. Doane, M.D., and Sidney O. Krasnoff, M.D.

Patient reported was a sixty-nine year old Russian male who was admitted to the Jewish Hospital on March 16, 1947 in an advanced stage of cardiac decompensation. His pulse rate on admission was 36 beats per minute and his blood pressure was 260/100. He presented evidences of a right hydrothorax, enlarged liver, and edema of both extremities. After a paracentesis was done and he was mildly digitalized, his pulse rate was 28–34. He exhibited a partial block which became complete, and which was on a two or three to one basis.

The first few days of his hospital stay he improved and was allowed to sit on the edge of his bed. He then exhibited typical Adams-Stokes attacks with unconsciousness, facial twitching, dyspnoea, cyanosis, and extreme bradycardia. These attacks could be produced at will by removing him from his oxygen tent. Two weeks after admission his systolic rate was discovered to be eight to twelve per minute. Strychnine, caffeine, and atropine produced no acceleration while ephedrin appeared to do so. He succumbed on the eighteenth day of his hospital stay, his pulse rate varying for the last twenty-four hours between eight and twelve.

At post-mortem no evident pathology was discovered in the heart which could be causative. Histologically, there was a calcareous plaque surrounded by collagenous material, below the membranous septum, distal to the bifurcation of the bundle of His. This involved both right and left bundles and was thought to be the cause of his difficulty. An electrocardiographic recording was made just prior and at the time of death.

Pathological Society of Philadelphia

Ernest E. Aegerter, President
Warner F. Sheldon, Secretary
R. P. Custer, Chairman, Program Committee

Proceedings of the Meetings, October, 1947–May 1948

Meeting, October 9, 1947

The Biological Mechanism of Carcinogenesis. I. Berenblum. (*No abstract supplied.*)

Meeting, November 13, 1947

Ulcerative Colitis in a Three Day Infant. Thomas K. Rathmell. (*Abstract 1, below.*)

Lesions Produced in the Chick Embryo by Monilia. Robert F. Norris, Winston K. Shorey, and Alfred M. Bongiovanni. (*Abstract 2, below.*)

Leydig Cell Tumors of the Testis in Mice. Hugh G. Grady. (*No abstract supplied.*)

Meeting, December 11, 1947

Paraffinoma of the Penis. William A. Ehrgott and Robert A. Bradley, Jr. (*Abstract 3, below.*)

The Histopathology of Lymphogranuloma Venereum. Edward B. Smith and R. Philip Custer. (*Abstract 4, below.*)

Meeting, January 8, 1948

A Study of the Golgi Apparatus and Mitochondria in a Series of Human Tumors. Albert E. Bothe, Willard S. Hastings, and Albert J. Dalton. (*Abstract 5, below.*)

Absence of Effect of Trypanosoma Cruzi Extracts (KR) on Malignant Mouse Tumors. Theodore S. Hauschka. (*Abstract 6, below.*)

Meeting, February 12, 1948

The Influence of Sex Hormones on Mammary Tumors Induced by 2-Acetaminofluorene. J. Stasney, A. Cantarow, and K. E. Paschkis. (*Abstract 7, below.*)

Problems of Calcification in Dental Tissues as Compared with Bone. Paul E. Boyle. (*Abstract 8, below.*)

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Diverticula of the Common Bile Duct. Julian Sterling. (*Abstract 9, below.*)

Investigations on the Mechanism of Caseation and Softening in Experimental Tuberculosis. Charles Weiss and Julius Schultz. (*Abstract 10, below.*)

Meeting, May 13, 1948

Involution of Lobules in the Senile Breast. Helen Ingleby. (*Abstract 11, below.*)

Gastric Neurilemoma. John Howard and Halvey E. Marx. (*Abstract 12, below.*)

Study of Bone Tumors in Animals. H. M. Martin. (*Abstract 13, below.*)

Abstracts

Abstract 1

Ulcerative Colitis in a Three-day Infant. Thomas K. Rathmell.

Adequate discussions of ulcerative colitis in adults are presented in text-books. The mechanism by which the ulcerative lesions of the colon are produced is not entirely clear. It has been shown in experimental animals that both bacteria and their toxins, as well as chemicals, may produce ulcerative colitis. The extent to which this knowledge may be applied to infants is unknown.

A case was presented of a three-day colored infant of normal birth, whose mother was not toxic and was serologically negative. No Rh factors were involved. The infant received an inunction of ammoniated mercury as a part of the routine birth care. It was breast-fed, with supplemental artificial feedings. The infant lost weight, developed clinical icterus, showed a temperature elevation and an erythematous rash 48 hours after delivery. It had one bowel movement consisting of mucus tinged with blood, and expired in 72 hours.

Routine postmortem examination showed icterus of the skin and endocardium, autolytic changes in the liver, areas of focal atelectasis in the lungs, and extensive discrete ulcerative colitis. Lesions involved the ascending, transverse, and descending colon. 48 ulcers were counted within a length of 14 cm. The non-ulcerated portions of the colon appeared relatively normal. There was intense autolysis of the tubular epithelium of the kidneys with definite glomerular damage. Toxicological studies for mercury were negative. Giemsa stain of the ulcerative areas of the colon disclosed bacilli both on the surface and in the base of the ulcers.

Ulcerative colitis in a three-day infant is regarded as a distinct anatomical and pathological entity of undetermined etiology which can be differentiated from epidemic diarrhea. Illustrations of the involved viscera were presented.

Abstract 2

Lesions Produced in the Chick Embryo by Monilia. Robert F. Norris, Winston K. Shorey, and Alfred M. Bongiovanni.

Eleven day old chick embryos were inoculated by the methods of Lee, Stavitsky and Lee on the chorioallantoic membrane, into the allantoic sac, and in the veins of the chorioallantoic membrane, with killed organisms of Candida albicans in concentrations of 1:200 by volume and with living organisms in various concentrations. Lesions of the embryo and membranes did not result from the inoculation of killed Candida by any of the three routes of inoculation. Lesions of the chorioallantoic membrane regularly occurred when suspensions of living Candida were injected intravenously or were inoculated on the chorioallantoic membrane or into the allantoic sac. Lesions of the embryo itself resulted only from intravenous inoculation of living organisms in concentrations up to and including 1:25,000 by volume. In both the chorioallantoic membrane and in the tissues of the embryo, the lesions were characterized by focal abscesses and granulomata. In embryos surviving for 2 days abscesses were accompanied by hemorrhage and by scanty infiltration with granulocytes and mononuclear phagocytes. In the lesions of embryos surviving for 3 to 4 days, the central areas of necrosis were associated with increased numbers of granulocytes and were surrounded by zones of proliferating reticuloendothelial cells, many of which were coalescing to form multinucleated giant cells containing phagocytized Candida. Fibroblasts in conspicuous numbers were also proliferating. The lesions therefore resemble those induced experimentally in laboratory animals and those which have been described in humans.

Abstract 3

Paraffinoma of the Penis. William A. Ehrgott and Robert A. Bradley, Jr.

A case of paraffinoma of the penis is reported in a 33 year old white male following an abrasion of the prepuce which was treated daily for six months with petrolatum. Microscopic examination of tissue from the penis and inguinal lymph nodes revealed a spongy appearance, the tissue being composed of various sized vacuoles, fibroblasts, and giant cells, the latter containing small vacuoles in their cytoplasm. Fat stains (Ciaccio, Osmic acid) were negative thereby proving that the oil was of mineral origin. A saponification procedure on the tissue disclosed a very low saponification number thereby further confirming the fact that the oil was of mineral origin.

Of interest is the fact that the patient in his occupation was exposed to cutting oils over

a period of seven years. Whether the tumor was caused by the topical application of petrolatum over a period of six months or by the occupational exposure to cutting oils is impossible to determine. It is believed that this is the first case of paraffinoma of the penis reported.

Abstract 4

THE HISTOPATHOLOGY OF LYMPHOGRANULOMA VENEREUM. Edward B. Smith and R. Philip Custer.

The major histopathologic lesions of lymphogranuloma venereum were discussed and various stages of their development illustrated by cases observed principally at the Army Institute of Pathology. The material included:

Penile lesions	13
Vulvar lesions	3
Lymph node lesions	531
Sinuses	
perianal	1
gluteal	1
inguinal	2
scrotal	1
Rectovaginal fistula	1
Diffuse pelvic inflammatory disease (female)	1

Emphasis was placed on the genital, genito-anal, ano-rectal and lymph node lesions. The suggestion of a causal relationship between the chronic ulcers of this disease and the development of squamous cell carcinoma was supported by the origin of a malignant tumor in one chronic vulvar lesion and by the pseudoepitheliomatous hyperplasia in several cases.

The quality of the inflammatory reaction was fairly uniform in the entire group, and the "stellate abscess" and "suppurative granuloma" were characteristic. However, these focal lesions have been simulated by chronic tularemia and have occasionally been found in lymph nodes where no etiologic factor was demonstrable. Consequently, the diagnosis of lymphogranuloma venereum should not be made on the basis of the histopathologic picture alone.

Abstract 5

A STUDY OF THE GOLGI APPARATUS AND MITOCHONDRIA IN A SERIES OF HUMAN TUMORS. Albert E. Bothe, Willard S. Hastings and Albert J. Dalton.

The almost constant presence of the Golgi apparatus and of mitochondria in cells lends interest to their observation under abnormal conditions, even though the nature and function of both are still matters of dispute. It was decided to undertake a study of these structures in a variety of human tumors. Material has been obtained from the operating room and small blocks placed at once in the appropriate fixing solutions. There have been over 150 neoplasms, with most of which uninvolved tissue of the same organ has been included. There have also been studied various hyperplasias not considered neoplastic, as well as many apparently normal tissues. A considerable part of the material has been from the genito-urinary tract. Acute inflammatory lesions have been avoided, owing to the complex factors within them and the practical difficulty of examining cells in an exudate. Most of the studies thus far have been of epithelial cells, since they normally have a more definite orientation and in general lend themselves more readily to cytologic study. Preliminary observations indicate that no one cellular entity may be used to characterize the neoplastic change. Neoplastic cells must be compared directly with the normal cell of origin in each case. In individual instances changes in the position and amount of the Golgi material have been noted. Changes in the size, form, and number of mitochondria have also been observed. Illustrative examples will be given.

Abstract 6

ABSENCE OF EFFECT OF TRYPANOSOMA CRUZI EXTRACTS (KR) ON MALIGNANT MOUSE TUMORS. Theodore S. Hauschka.

The claims of Roskin and Klyueva, concerning the cancerolytic properties of living T. cruzi and T. cruzi lysates, were not borne out by our experiments with 8 different strains

of T. cruzi and 5 varieties of malignant tumors in over 1300 mice. Among the trypanosomes tested was the "Wellcome—BH" strain, used by the Russians, and the "Soule" strain, on which Malisoff based his recent positive results. Exact repetition of Malisoff's work, but with adequate controls, showed that his transplantable mouse sarcoma T-180 regressed spontaneously in about 55% of the untreated mice. Tumor regressions among the T-180 mice treated with Malisoff's modification of KR (whole culture lysates) were about 50%. Whole culture lysates of "Soule" strain T. cruzi had no effect on the growth of spontaneous mammary adenocarcinoma in C_3H- and dba-mice. The present state of KR investigation in this country holds out no clinical promise.

Abstract 7

THE INFLUENCE OF SEX HORMONES ON MAMMARY TUMORS INDUCED BY 2-ACETAMINOFLUORENE. J. Stasney, A. Cantarow, and K. E. Paschkis.

The present report deals with the influence of estrogen, androgen, and progesterone upon the development of mammary tumors in rats receiving 2-acetaminofluorene in their diet. The incidence of mammary carcinoma in non-breeding female rats receiving 2-acetaminofluorene was 24%, which was not increased by simultaneous administration of estrogen, but was increased enormously by progesterone (82%). Breast tumors, absent in carcinogen-treated males, appeared in small percentage receiving estrogen and in one receiving testosterone.

The data suggest that small amounts of estrogen are probably necessary for the development of breast carcinoma in rats treated with 2-acetaminofluorene, but that the quantity of progesterone may be the limiting hormonal factor in this connection.

Abstract 8

PROBLEMS OF CALCIFICATION IN DENTAL TISSUE AS COMPARED WITH BONE. Paul E. Boyle.

The calcified dental structures, cementum, dentin and enamel, differ from bone in that they do not serve as a physiologic reserve of calcium salts. Formation of matrix and calcification are one way processes not subject to reversal. The dental structures, therefore, constitute a delicate and permanent record of metabolic disturbances affecting matrix formation and calcification during the period of tooth formation. The effect of ascorbic acid deficient diets in specifically retarding the formation of dentin was demonstrated. Enamel matrix, of epithelial origin, was relatively unaffected in man, monkey and guinea pig.

The calcification of tooth structures in animals on diets deficient in calcium and vitamin D was compared with the calcification of bone. Wide uncalcified seams in developing teeth (dentinoid) are characteristic of low calcium rickets as well as low phosphorus rickets, whereas osteoid is characteristic only of the latter.

The iron containing pigment of rodent incisor teeth was discussed as a method of following microscopically the concentration in cells and eventual deposition in an extracellular matrix of mineral salts.

Electron photomicrographs of the crystallite components of enamel were shown. The crystallites are 40 to 60 millimicrons in diameter. It was suggested that the relative unavailability of calcium salts from dental structures may be due to differences in size or arrangement of the crystallites from those in bone.

Abstract 9

DIVERTICULA OF THE COMMON BILE DUCT. Julian A. Sterling.

Abnormal channels in the terminal portion of the common bile duct were found in seven per cent of a series of seventy anatomical dissections. Four diverticula of the common bile duct and one choledocho-pancreatic duct fistula were observed. Two diverticula contained biliary calculi. In these, there was gross and microscopic evidence of pancreatitis. One specimen which presented severe pancreatic necrosis adjacent to a diverticulum did

not present calculi at post-mortem examination, although there was a past history of cholecystectomy for cholelithiasis. Diverticula of the common bile duct may be a factor in the pathogenesis of certain forms of pancreatitis.

The diverticulum in the terminal portion of the common bile duct is easily overlooked. It was recommended that careful dissection be done in the preserved specimen in cases presenting a past history of pancreatitis.

Abstract 10

Investigations on the Mechanism of Caseation and Softening in Experimental Tuberculosis.* Charles Weiss and Julius Schultz.

Rabbits which were injected intratracheally with virulent Ravenel tubercle bacilli were killed five weeks and four months after infection. Nitrogen and benzoylarginineamide (BAA) peptidase content were determined on homogenates of the lungs, liver, kidneys and spleens of these animals. The data were compared with results on controls sacrificed at the same time. No significant conclusions could be drawn fron these results when expressed in terms of enzyme concentration. In the case of the lungs, however, total enzyme content, expressed as a function of the body surface, was increased above the normal both at five weeks and four months after infection. It appears that more enzyme enters the lung as the infection progresses and caseation develops. The significance of these results lies in the fact that the presence of five to ten times the lung mass, consisting mostly of caseous material, does not produce a dilution or diminution of enzyme activity per unit mass. The nature of the factors involved are discussed and it is suggested that either the caseous material itself contains active cellular particulates or that the cells which are concerned in the formation of caseous material may be five to ten times more active than those of normal lung cells.

It is also pointed out that this is the third instance in which an increase in proteolytic enzyme activity is associated with an increased resistance to infection.

New methods were described for the determination of the rate of hydrolysis of BAA by tissue homogenates and of the rate of hydrolysis of leucylglycylglycine by serum.

* Aided by grants from the National Tuberculosis Association and the Tuberculosis Study Section of the U. S. Public Health Service, National Institute of Health.

Abstract 11

Involution of Lobules in the Senile Breast. Helen Ingleby.

The pattern of involution seen in lobules during the menstrual phase is not the only type of involution that occurs in the human female breast. Growth and regression continue after the menopause but are of course not cyclic in character. The microscopic features of this involution differ essentially from those characteristic of the sexual cycle. In the affected ductules the cells undergo hyaline degeneration and fuse; the nuclei lose their structure; they persist for a time, but eventually all that remains is a hyalinized nodule. This process may take place in a group of ductules. Those at the periphery may be affected first. The central duct sometimes escapes. When this happens the central duct will be surrounded by a hyalin band. Hyalinization of ductules is common in mammary dysplasia and explains the picture of a central, more or less degenerated, ductule surrounded by a hyaline band which is so often seen in this condition. Malignant cells may degenerate in the same way and with suitable staining it can be shown that the hyaline material seen in so-called "scirrhus carcinoma" is derived from degenerated tumor cells. This type of degeneration appears to be accelerated by the administration of stilbesterol. It remains to be seen whether it will be possible to evaluate the efficacy of stilbesterol in any given case by examining the pattern of degeneration in the tumor to be treated.

Abstract 12

GASTRIC NEURILEMOMA. John W. Howard and Halvey E. Marx.

Neurilemomas of gastric origin and of the retroperitoneal space near the stomach are uncommon in the literature. More critical diagnosis may prove them to be more common than is suspected.

Previously these tumors may have been reported as neurinomas, perineural fibroblastoma and sarcoma. They are thought to have ectodermal neurogenic origin from the cells of the Sheath of Schwann or to arise from mesodermal fibroblasts. Stout proposed the term neurilemoma in 1935.

There are two histologic types of this tumor. Verocay's neurilemoma is the more characteristic because of the presence here and there of groups of tumor cells with nuclei arranged in parallel and opposing palisades and with their connecting cellular processes appearing not unlike a mass of collagen between the rows of nuclei—"The Verocay Body".

Antoni's neurilemoma is much less orderly and more like a myxoma or a neurofibroma. This form does not produce the characteristic Verocay bodies and may be identified by the cells which are more delicate and smaller than the fibroblast.

Grossly these tumors frequently appear encapsulated and are often yellow orange or grey in color. They are rubbery and firm, and they usually measure 1–3 cm. in diameter, some may grow much larger.

Four cases, three males and one female, of neurilemoma probably of gastric origin are presented with roentgenological and microscopic findings.

Abstract 13

STUDY OF BONE TUMORS IN ANIMALS. H. M. Martin.

Tumors of bone are not the most common group of neoplasms encountered in our domestic animals. However, they cannot be considered as rare, especially in carnivorous (domestic) animals. In this series of bone tumors only two occurred in herbivorous animals. Of the 29 cases only three were benign.

The location of the primary growths in the 26 malignant tumors was quite variable. Of the seventeen malignant growths studied in the dog, five occurred in the flat bones and twelve in the long bones. All but one of the latter group occurred near the extremities. However, in the eight cat cases only three occurred in long bones. The five remaining originated in the flat bones of the head.

In this group of bone tumors the writer observed representatives which fall into the following general classification; osteogenic, chondrogenic, and giant cell series with one Ewing's sarcoma of bone.

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Resignations

Goforth, J. L. (1948)
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Deaths

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Life Situations, Emotions and Gastric Function

A Summary*

By STEWART WOLF, M.D., AND HAROLD G. WOLFF, M.D.

THE data in this communication are derived from observations on Tom, a fistulous subject observed closely for over five years (1) and three other men whose gastric fistulae were performed as a preliminary to the removal of a carcinoma of the esophagus. Tom underwent gastrostomy in 1895 because of a benign stricture of the esophagus consequent upon swallowing scalding hot clam chowder. His hole is larger than that of William Beaumont's famous patient, Alexis St. Martin. In Figure 1 is shown the subject reclining on the laboratory table. Mid-way between the umbilicus and xiphoid is the stoma. Through it has herniated a collar of gastric mucosa.

Method

For more than a year successive daily observations were made on the stomach of this subject throughout the four hours of the morning. An immediately striking finding was a wide variation from day to day in color and turgidity of the mucous membrane. The color varied from a pale orange-pink to a vivid cardinal red. It was recorded in terms of a color scale calibrated in figures from 20 to 100 (2). Associated with the color changes there occurred changes in the turgidity of the membrane. These could be estimated roughly by the number of folds seen in the collar of redundant gastric mucous membrane. In general, the redder the membrane the more turgid and the fewer folds which could be counted. Observations of motor activity were made by the familiar technique of introducing a distendable balloon into the cavity of the stomach and recording pressure changes in a water-manometer on a moving kymographic drum. Figure 2 shows how body movements were distinguished from actual gastric contractions by means of a spirometer attached around the body near the lower rib margin. Gastric juice was continuously siphoned from the stomach through a Levine tube and specimens analyzed at fifteen minute intervals for free and total acidity. Measurements of volume were made together with observations of the gross appearance of the gastric juice. A rough calculation of the actual output of hydrochloric acid was made by a method

* Based on a paper, entitled "Emotional Factors in Gastro-intestinal Tract Disease", read by Dr. Stewart Wolf at the meeting of the College of Physicians of Philadelphia, Section on General Medicine, 26 January 1948.

From the Departments of Medicine and Psychiatry of The New York Hospital and Cornell University Medical College.

derived from the work of Hollander (3) and described in an earlier publication (1). By a device pictured in Figure 3, the blood flow through the stomach was measured and it was found that color changes paralleled changes in blood flow. The redder the stomach the greater the flow of blood through the membrane (4).

FIG. 1. VIEW OF PATIENT RECLINING ON LABORATORY TABLE. NOTE GASTROSTOMY OPENING MIDWAY BETWEEN UMBILICUS AND XIPHOID

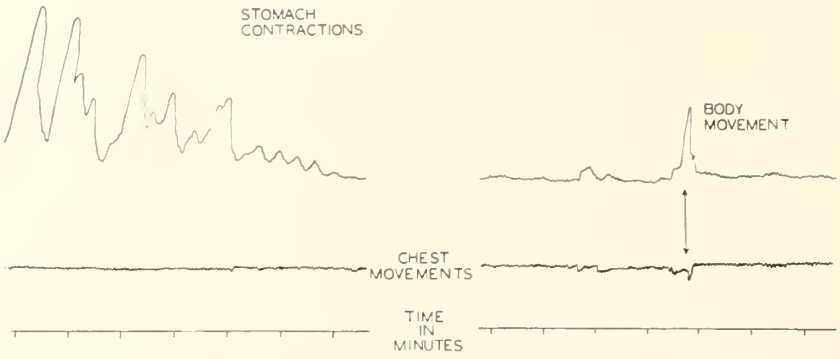

FIG. 2. DIFFERENTIATION OF ARTIFACTS FROM ACTUAL CONTRACTIONS OF THE STOMACH WALL BY MEANS OF A SIMULTANEOUS PNEUMOGRAPHIC TRACING FROM THE LOWER MARGIN OF THE CHEST

OBSERVATIONS

It was found that in general hyperaemia of the gastric mucous membrane was associated with both increase in acid production and increase in motor activity, while pallor of the membrane was accompanied by a diminution in these two functions. See Figure 4.

APPETITE

Separate from the painful sensory experience of hunger, but regularly associated with it is the emotion or feeling state called appetite. The awareness of a pleasant relationship to food is one of a group of situations which give rise alike to emotional variations and variations in gastric function. In Figure 5 are shown the changes in gastric function which were found to occur when the subject of appetizing food was discussed or when such food was tasted.

FEAR

The "sinking feeling" in the stomach which accompanies fear is another familiar psycho-

somatic phenomenon. Intense fear is often accompanied by nausea. Figure 6 illustrates a situation in which sudden fear occurred one morning during the control period of ac-

attached great importance. Our subject, who tidies up the laboratory, had mislaid them the previous afternoon and he was fearful of detection and of losing his precious job. He

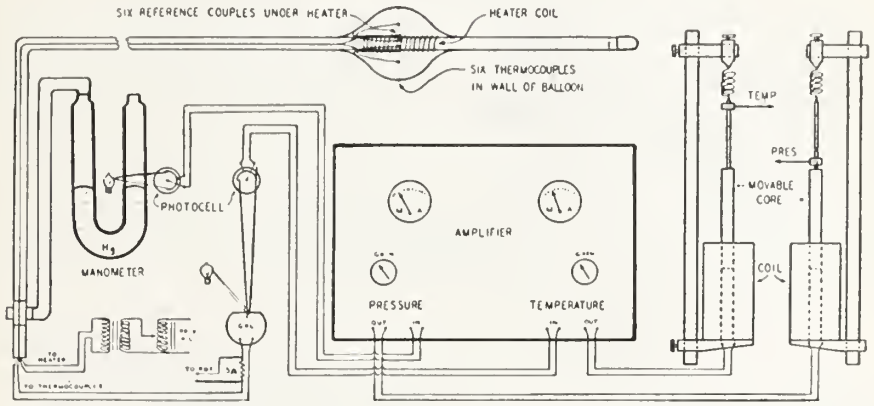

FIG. 3. A DIAGRAM OF THE THERMAL GRADIENTOMETER FOR THE MEASUREMENT AND RECORDING OF GASTRODUODENAL BLOOD FLOW

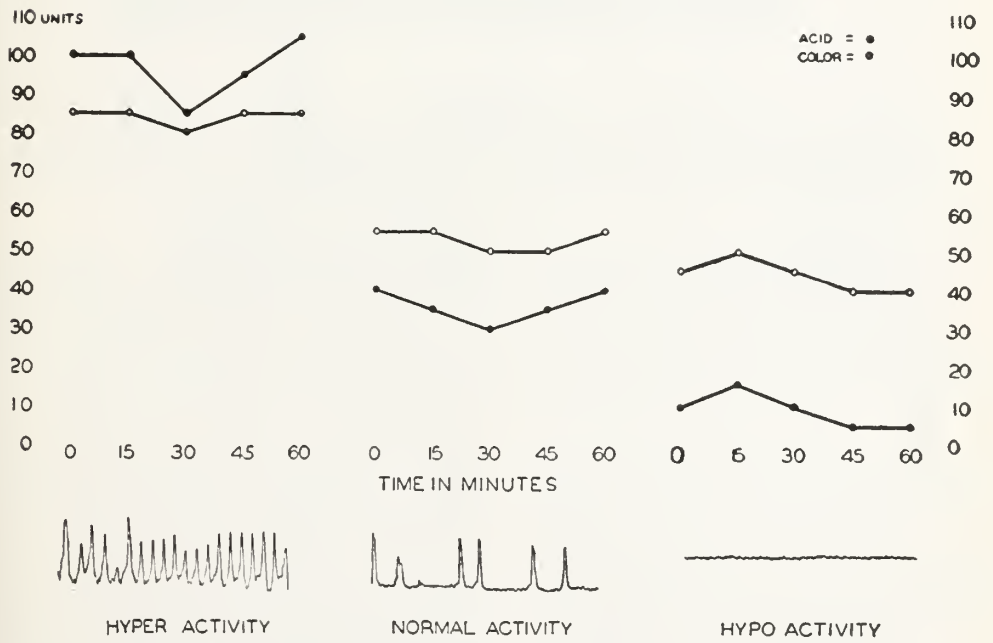

FIG. 4. CORRELATION OF COLOR OF GASTRIC MUCOSA WITH GASTRIC ACIDITY—MOTOR ACTIVITY

celerated gastric function, when an irate doctor, a member of the staff, suddenly entered the room, began hastily opening drawers, looking on shelves, and swearing to himself. He was looking for protocols to which he remained silent and motionless and his face became pallid. The mucous membrane of his stomach also blanched from a level of 90 to 20 on the color scale and remained so for 5 minutes until the doctor had located the ob-

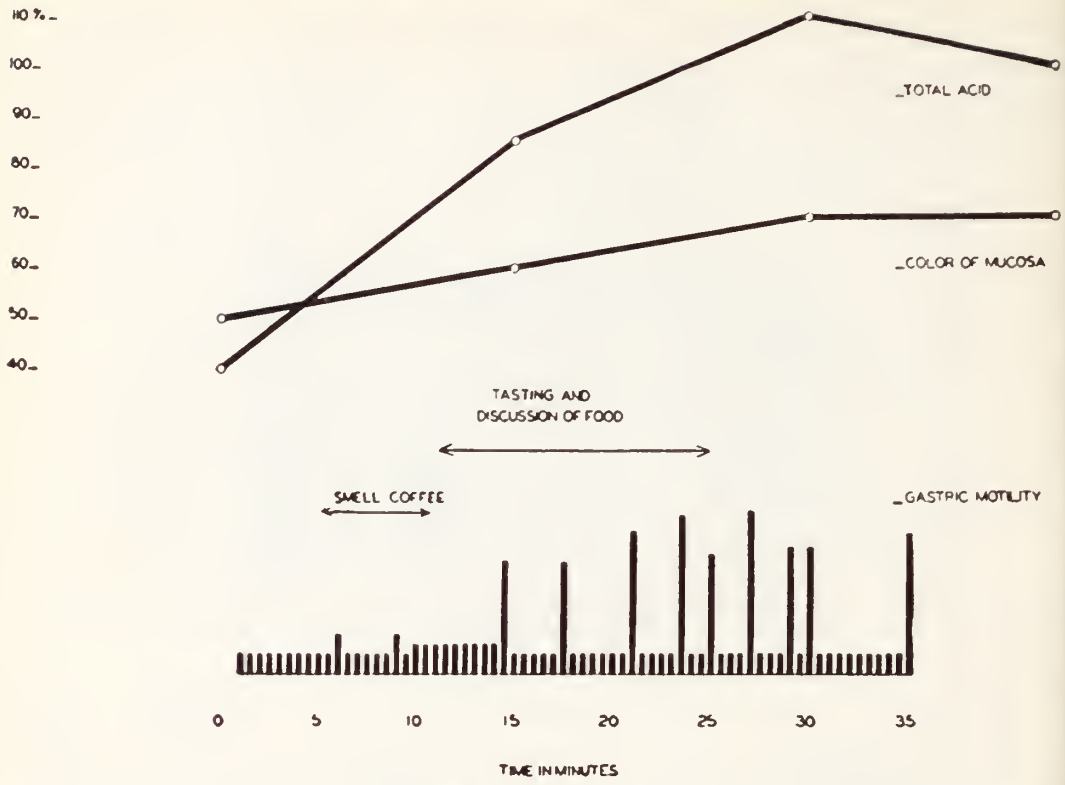

FIG. 5. CHANGES IN GASTRIC FUNCTION ACCOMPANYING APPETITE. THE FREQUENCY, HEIGHT AND DURATION OF GASTRIC CONTRACTIONS IS REPRESENTED SCHEMATICALLY ON THE LOWER PART OF THE GRAPH

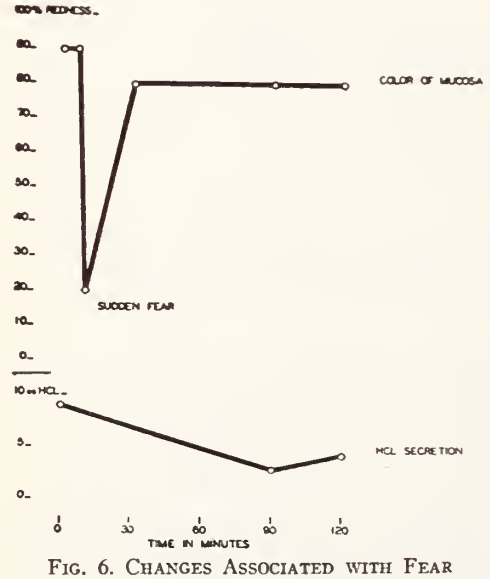

FIG. 6. CHANGES ASSOCIATED WITH FEAR

jects of his search and left the room. Then the gastric mucosa gradually resumed its former color.

DEJECTION

Other emotions besides fear which imply a feeling of being overwhelmed and defeated such as for example, sadness and dejection may be accompanied by anorexia "sinking in the stomach" and nausea. Such a circumstance is illustrated by another disturbing event which occurred in Tom's life, namely, the death of his favorite nephew, the son of his most beloved sister. Tom's main affect was one of dejection. He didn't want to face the event. The same day his youngest step-grandson became ill with mumps. The following morning, during the experimental period, Tom said, "I don't relish much going down there tonight, (the house of his sister). "I don't mind the funeral—but the wake! I told my wife somebody should stay with the grandson who got mumps, so I figured that she and my daughter could go down to my sister's and when they had enough, I could go down later.

It doesn't matter how late I get home." Tom was noticeably pale and looked a little haggard, although he made an attempt at gaiety and buoyancy. He had no appetite. "I just feel funny—full. I don't want to eat." After the acceleration of gastric secretion induced by his breakfast had worn off, there was no free acid, and only approximately 10 units of total acid. During the last three collection periods the amount of juice obtained was too small for titration. Only 40 cc. of saliva was produced in two and a half hours, less than two-thirds the usual amount.

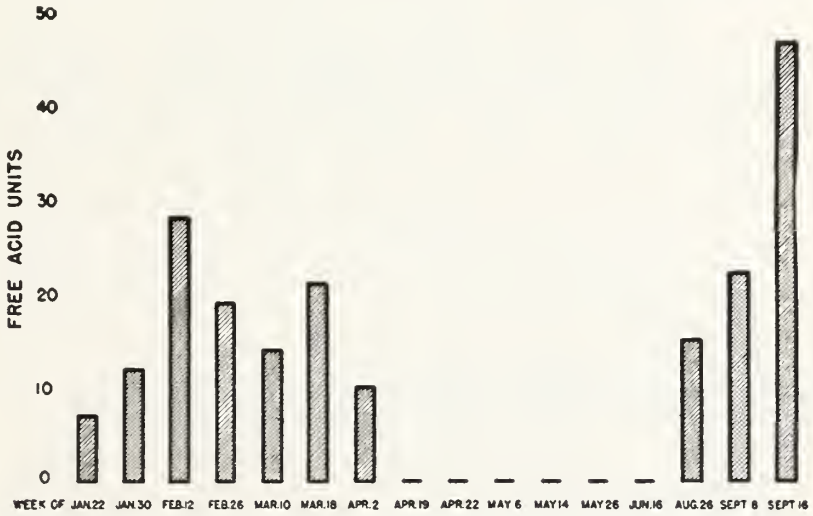

Fig. 7. A Persistence of Gastric Anacidity for Two Months During Overwhelming Fear and Dejection Each Column Represents the Weekly Average of Determinations of Free Acid Made Daily

Comment: Gastric hypofunction accompanying fear or dejection was regularly associated with a diminution in the flow of saliva as well as of gastric juice. When, in a setting of disgust or guilt with feelings of rejection, there occurred nausea in association with pallor, inactivity and diminished acid secretion in the stomach, an accompanying increase in salivary flow, as well as apparent acceleration of secretion of gastric mucus was observed.

The line of demarcation between these two types of gastric hypofunction is not entirely clear, except as indicated by the presence or absence of nausea. As has been shown elsewhere (5) nausea, however induced, is associated with absence of contractile activity in the stomach, diminished acid secretion but increased output of mucus.

SUSTAINED GASTRIC HYPOFUNCTION

Gastric hypofunction was not included in Tom's habitual way of reacting to threats. Occasionally, however, when he felt thoroughly defeated or overwhelmed by a situation he did display gastric hypofunction for longer or shorter periods. On one occasion this pattern was sustained for two months associated with anorexia, taciturnity, loss of drive and weight, loss of 12 pounds. One set of experiments involving continued suction on an indwelling duodenal tube was particularly distasteful and frightening to Tom. His fear and feeling of helplessness were accentuated when one day a technician in whom he had never had full confidence, drew blood through the suction apparatus in the duodenum. As shown in Figure 7 Tom's stomach contained no free HCl for 10 months until a job was secured for the technician in another hospital. The day after she left acid reappeared in the gastric samples. Appetite returned and Tom again

became his jovial, energetic, quick moving self.

GASTRIC HYPOFUNCTION AND DISEASE

Certain individuals seem to react to threats characteristically by a pattern of alarm and withdrawal, rather than fighting back. Such attitudes are associated with feelings of hopelessness and defeat. Illustrative of such a pattern is the case of a 24 year old single female, a stutterer who came to The New York Hospital complaining of fullness in the epigastrium associated with anorexia and nausea. She had been rejected by both parents, had reacted to life problems with indecision and had attempted to resolve them by rationalization rather than by action. She felt that her own security and that of the Jews in general depended heavily upon the success of the Zionist movement. She was intubated with a gastric balloon and with another tube through which specimens of gastric juice were collected. The balloon was inflated in the stomach and connected to the kymograph. During a phase of gastric contractions of average frequency and amplitude, her attention was called to a newly formed society dedicated to opposing the Zionist movement and exposing what they considered misrepresentations by the Zionists. She had not previously heard of the society, and she appeared horrified to learn of their activities. Pale and wide-eyed she stared at the examiner, immobile and obviously frightened. The motor activity in her stomach promptly stopped. The organ relaxed and increased in size. Finally nausea occurred. The gastric changes are illustrated graphically in Figure 8. Later discussion revealed that this individual characteristically reacted to threatening situations with anxiety in which there were strong feelings of hopelessness and despair.

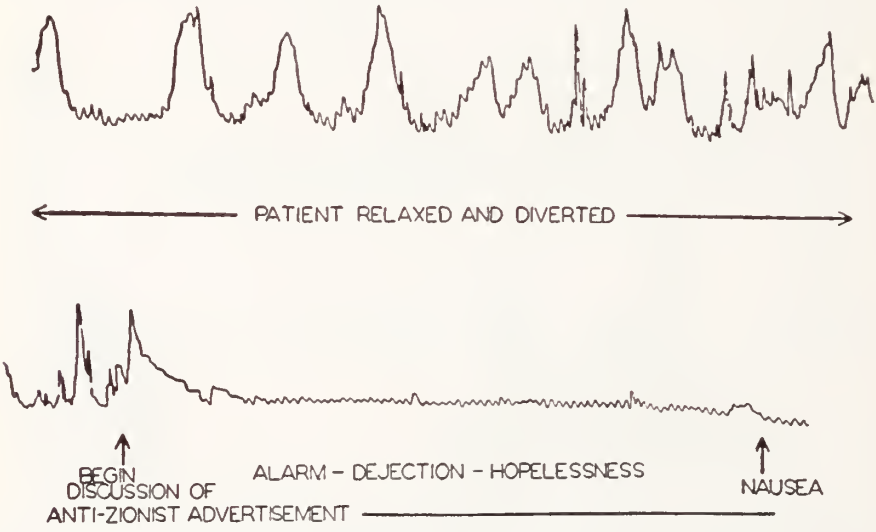

FIG. 8. SUDDEN INTERRUPTION OF GASTRIC CONTRACTIONS FOLLOWED BY NAUSEA UPON EXPERIENCING FEELINGS OF ALARM, DEJECTION, AND HOPELESSNESS

"When something comes up to worry me, I have a feeling of being defeated, that things are hopeless. That is how I felt when you showed me that advertisement of the anti-Zionist organization."

Comment: This type of gastric disturbance seen commonly among soldiers in the horrifying anxious circumstances of combat (6) was recognized several years ago by Walter Cannon (7) and it was long thought to be the only way in which the stomach reacted during stress. In recent years, however, numerous workers have shown that as the face may blanch or blush in varying situations of stress, so may

the stomach become either hypoactive or hyperactive, depending on the situation and the individual.

GASTRIC HYPERFUNCTION, ANGER AND RESENTMENT

Tom is a man of Irish extraction, small, wiry, energetic, conscientious and friendly, but sensitive and easily offended, especially by slights to his proficiency and effectiveness as a worker, provider or head of the family. He usually reacted to menacing situations by anger, resentment and accelerated general activity as well as with gastric hyperfunction.

An example of the changes in motor activity and acid secretion which accompanied feelings of resentment and hostility occurred during an experimental period when a spontaneous phase of accelerated gastric activity had subsided an hour before and another would not be expected for at least one and one-half to two hours later. The parietal secretion and blood flow had not quite fallen to their control level, although contractions had decreased nearly to a minimum with waves less than 1 cm. high on the recorded tracing. At this moment a doctor for whom Tom had been engaged to do piecework housecleaning after hours entered the room. As he entered Tom flushed a little, because he resented the past attitude of that doctor towards his work. The latter had insinuated that Tom's charges were excessive and that he worked too slowly. The doctor came to pay him off and tell him that his services were no longer required. Tom did not mind so much losing the work but he was angry and hostile about the aspersions cast upon his abilities and conscientiousness. He felt humiliated and resentful. His face was red and his collar seemed too tight. The gastric mucosa became hyperaemic and engorged and acid production was more than doubled. Vigorous contractions began and his stomach presented an appearance of overactivity similar to but less marked than that encountered in experimentally induced gastritis (8). See Figure 9.

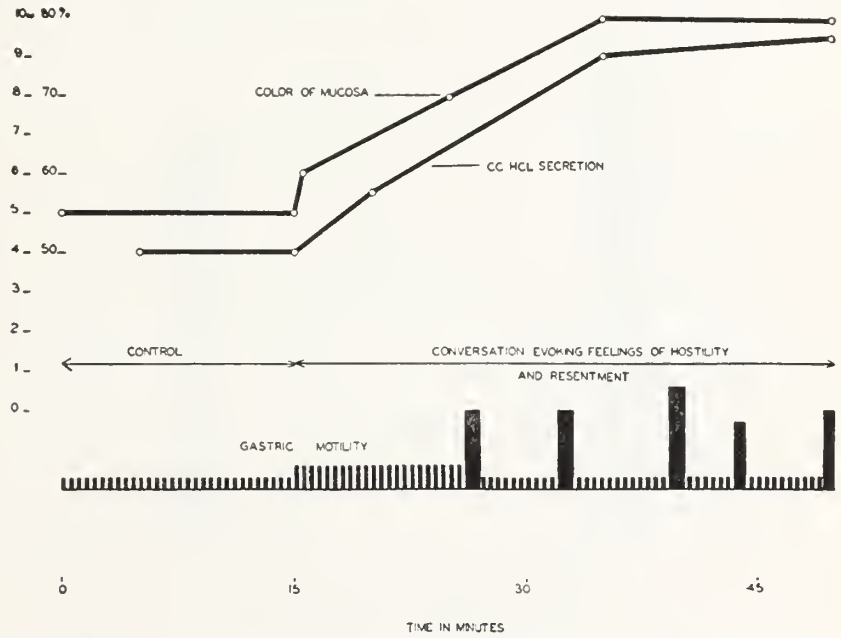

FIG. 9. INCREASED MOTILITY ACCOMPANYING HYPERAEMIA AND HYPERACIDITY IN ASSOCIATION WITH HOSTILITY AND RESENTMENT

SUSTAINED RESENTMENT

Tom's injuries were always either dealt with or relatively quickly forgotten, and never

were gastric disturbances unduly sustained, except occasionally during periods of special stress as, for example, on an occasion when a certain benefactor on whom Tom depended partially for livelihood threatened to withdraw his support in view of Tom's decision to incorporate into his family the four children of his stepdaughter. Following the latter's death some months before, the children had been unhappily situated in an orphan home. Despite his benefactor's attitude, Tom persisted in his determination to undertake the additional responsibility of caring for the children. His reaction to this threat to his security was characterized by resentment at the interference with his personal affairs and seeming discrimination against him, and anxiety about his economic welfare. During this period of stress the average basal secretion of acid was significantly higher than during the preceding two weeks, and his membrane was continuously engorged and reddened. He was most eager to throw off his dependence on this person, and when a new source of revenue became available in the form of increased pay from the hospital, two weeks later, he did so with great relief. Again his acid production and vascularity returned to former levels. The changes are illustrated in Figure 10.

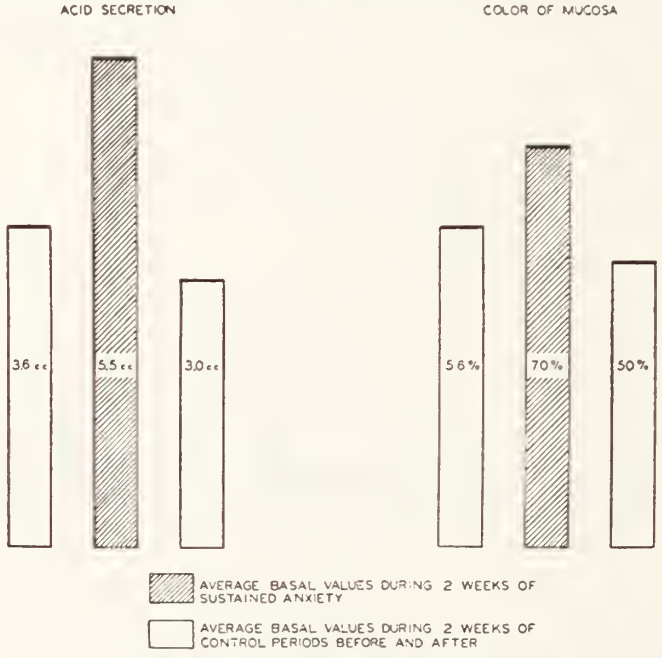

FIG. 10. SUSTAINED ACCELERATION OF GASTRIC FUNCTION DURING CHRONIC EMOTIONAL CONFLICT

HAZARDS OF SUSTAINED MUCOSAL ENGORGEMENT

In the gastric mucosa of Tom, it was shown that sustained gastric hyperfunction gave rise to two potentially serious conditions in the lining of the organ, namely, a lowering of pain threshold, and an increase in fragility. Ordinarily, no pain was felt when noxious stimuli such as pinching, or faradic current were applied to the gastric mucosa. Likewise under average circumstances the mucosa was impervious to blows from a blunt glass rod or to other minor traumata. Under circumstances of sustained engorgement, however, pinching, and the application of faradic current were painful, and erosions and hemorrhagic spots resulted from minor traumata. Figure 11 illustrates one way in which a potential hazard from this situation was shown to exist. Two small hemorrhagic lesions were

kept in contact with gastric juice with a titratable total acid of 90 for half an hour. Mucus accumulated rapidly in the region, but it was removed at frequent intervals by suction through a small glass tube. The acid gastric juice was then reapplied to the bare mucosa. A sharp acceleration of acid and concomitant hyperaemia of the whole stomach mucosa occurred and persisted for half an hour after the submersion of the haemorrhagic lesions were discontinued.

EXPERIMENTAL PRODUCTION OF ULCER

The most peripheral edge of the collar of mucosa which lay exposed on the abdominal wall lacked adequate protection owing to defective formation of mucus in this region. A small erosion which occurred on this peripheral edge was exposed continuously to the digestive action of gastric juice for four days. During the first 24 hours the denuded surface increased in size. It bled intermittently. At the end of four days it exhibited the typical punched-out appearance of chronic peptic ulcer with well-defined edges and a granulating base. It measured approximately 4 mm. in diameter, 1 mm. in depth, and was growing rapidly (Figure 12). Traction or pressure on this lesion resulted in pain of a dull, gnawing character, which was localized in the region of the lesion itself. Throughout the four-day period the whole mucosa was relatively engorged, and the rate of acid secretion was significantly elevated.

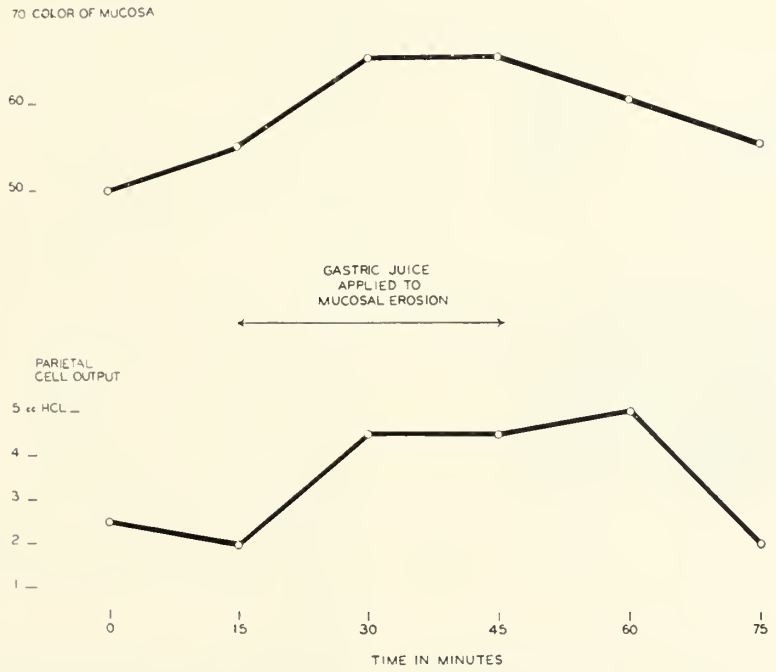

FIG. 11. THE ACCELERATION OF ACID PRODUCTION FOLLOWING CONTACT OF GASTRIC JUICE WITH AN ERODED MUCOSA

Comment: In this phenomenon may lie an explanation of the persistent hyperacidity regularly encountered in persons suffering from gastritis and peptic ulcer. The fact that the base of the ulcerated lesion which is constantly bathed in acid gastric juice effects a stimulation of acid secretion indicates that afferent impulses subserve this reflex without sensation resulting. It is likely, however, that pain would follow an adequate chemical stimulus (9).

At the end of four days because of the hazard to the subject it was felt that the experiment could not be allowed to continue.

The ulcer and surrounding area were covered with a protective petrolatum dressing. Within three days, complete healing had taken place, leaving no trace of the lesion behind.

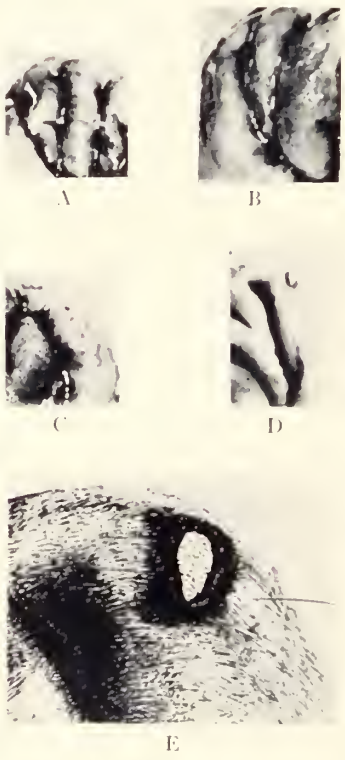

FIG. 12.

A. NORMAL MUCOSAL FOLDS DURING CIRCUMSTANCES OF SECURITY AND CONTENTMENT

B. SAME FOLDS DURING HYPERAEMIA AND ENGORGEMENT OF GASTRIC MUCOSA ASSOCIATED WITH EMOTIONAL CONFLICT INVOLVING HOSTILITY AND RESENTMENT

C. SMALL MUCOSA EROSION COVERED BY BLOOD-STAINED FLAKE OF OPAQUE MUCUS OCCURRING IN ENGORGED HYPERACTIVE STOMACH

D. SMALL PUNCHED-OUT ULCERATION INDUCED BY THE ACTION OF GASTRIC JUICE ON AN AREA INADEQUATELY PROTECTED BY MUCUS.

E. DRAWING OF ULCER (OF D.) ENLARGED

CLINICAL PEPTIC ULCER

Patients with peptic ulcer habitually react to stress by intense and sustained gastric hyperfunction. An example of such a reaction is provided by a 44 year old civil service employee who had complained of gnawing epigastric pain off and on for 20 years. His father had been a gentle retiring person and his mother a matriarchal woman intensely ambitious for her children. His two older brothers were able to adjust satisfactorily to this setting, the oldest by graduating from medical school, the second one by adopting a rebellious attitude and becoming a professional gambler instead of a lawyer as his mother had wished. The patient felt the need to compensate for his brother's indifference and took pre-medical work in college. He did poorly, and tried engineering instead. After failing that he abandoned college. In this setting he had his first symptoms of epigastric pain and a duodenal ulcer was demonstrated by radiologic examination. He later obtained a civil service job as a draftsman and became engaged to a warm, sympathetic girl. Symptoms disappeared during this interval until the girl died of rheumatic heart disease a few months later. The patient's mother also died at approximately the same time. Within a few months he married an authoritarian, cold and financially ambitious woman. She disapproved of his social relationship with men friends, and eventually forced him to give up lodge activities from which he derived great satisfaction.

Shortly after his marriage the patient's ulcer symptoms recurred and they have remained chronic ever since. Several exacerbations and two episodes of hemorrhage have coincided with periods in which his wife seriously disparaged his competence as a man.

The following experiment shown graphically in Figure 13 illustrates the relevance of his conflicts concerning his wife to his gastric disturbance.

Ten minutes after the end of a spontaneous period of vigorous gastric motor activity and during a period of almost complete absence of contractions an interview was undertaken in which the patient was reminded that in contrast to the high regard in which he had been

held by his lodge associates, his wife considered him inadequate as a provider, companion and sexual partner. He became grim and tense, clenched his jaws frequently and said, "It's been a fight all along and now I got no more fight left in me. I'm caught like a rat in a trap." Promptly, forceful gastric contractions began and by the end of the interview a state of incomplete tetanus had been established. Acid secretion was also greatly enhanced, exceeding the level observed during the earlier period of spontaneously increased gastric function. By this time the subject had begun to groan with pain.

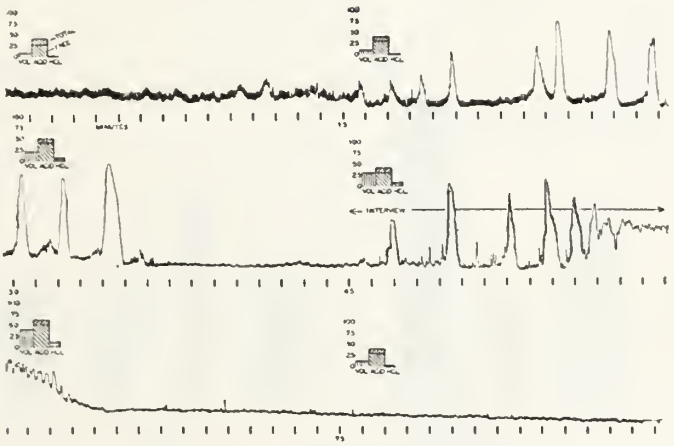

FIG. 13. CHANGES IN GASTRIC SECRETIONS AND MOTOR ACTIVITY INDUCED DURING DISCUSSION OF RELEVANT CONFLICTS

Shortly, thereafter, during attempts at reassurance and diversion, the evidences of gastric hyperfunction subsided and with them the symptoms.

MECHANISM OF GASTRIC HYPERFUNCTION

The pathways whereby the impulses responsible for this type of gastric hyperfunction reach the stomach are unknown but have been suspected of lying in the vagus nerves. Confirmation for this notion derives from an experiment performed on one of the fistulous subjects whose fistula was made prior to the performance of a surgical removal of a carcinoma of the esophagus (10). During the latter procedure it was necessary to section the vagus nerves. Thus, direct observations were available on the stomach before and after vagotomy. On coming to the laboratory for the third experiment, and prior to vagotomy, a marked change in the appearance and manner of the subject was noted. Earlier he had behaved in a quiet, friendly manner. On this occasion his face was red and he appeared somewhat exasperated and irritable. He complained of stiffness and back pain ever since the previous experiment and confessed that he was angry at having to come down to the laboratory again in view of the apparent delay occasioned in his operation.

The subject's stomach was examined and found to be much redder and more engorged than before, about 70 on the scale in contrast to the previous 50. He was more voluble and talkative. Asked about his concern regarding his condition, he said that he was reminded of the first doctor whom he had consulted for difficulty in swallowing. The latter had focussed his attention on the stomach, much to the annoyance of the patient. "He was so dumb; I told him it wasn't in my stomach, because I knew I couldn't swallow right. He made me waste four weeks fooling around." On this occasion there occurred much more spontaneous motor activity in the stomach than before. The mucous membrane was so

turgid that the minor traumata incident to the instrumentation with the cystoscope caused bleeding. The subject's dominant mood during this interview was anger coupled with hostility and strong feelings of frustration. His stomach displayed the picture of hyperactivity so characteristically found in the subject, Tom, during situational conflicts productive of aggressive attitudes.

Approximately three weeks following vagotomy an opportunity was afforded to repeat these observations under similar circumstances. On the third experimental occasion following vagotomy, the membrane was pale, 40, and the folds appeared especially thin. After the baseline observations, an attempt was made, as before, to induce anger and resentment in the subject by discussion of the doctor who had failed to diagnose his condition when he first consulted him. As on the occasion prior to vagotomy, he appeared to become significantly angered with flushing of the face, loud voice and aggressive gestures. "I think he is crazy. I only went to him because he is around the corner. He said the lining was off my stomach and gave me some stuff that made me feel lousy. . .last winter I had some crushed toes. He messed them up, too. He's a God-damned quack, an exile. He charged me enough—$8.00 a treatment. I'll tell him off." During this outburst the patient's stomach was continuously under observation through the cystoscope, but despite the redness of his face, there occurred no detectable change in the appearance of his gastric mucosa. See Figure 14.

Comment: Failure of the stomach to become engorged during such a state does not necessarily implicate the vagus as a route by which impulses responsible for gastric hyperfunction occurring in response to situational threats reach the stomach. The evidence is highly suggestive, however, especially when considered in company with the clinical results of the treatment of peptic ulcer by vagotomy.

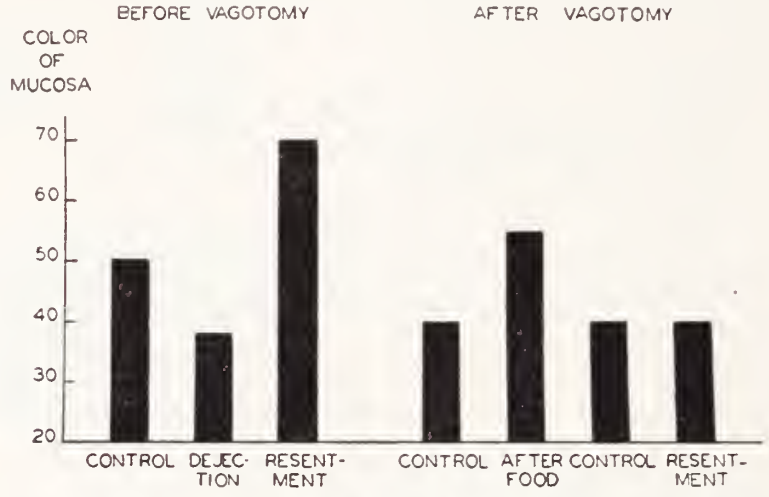

Fig. 14. Variations in Color of the Gastric Mucosa under a Variety of Circumstances before and after Vagotomy

Protective Mechanisms in the Stomach

One biological defense against the completion of the unsalutary chain of events which apparently predisposes to peptic ulcer is an inhibitory effect on gastric secretion of acid and a promotion of mucus secretion which occurs in response to the introduction of strong acid into the cavity of the stomach. This effect is illustrated graphically in Figure 15.

20 cc. of 0.1 N hydrochloric acid introduced into the stomach during a phase of moderately active secretion inhibited further acid production and stimulated the elaboration of

mucus with the result that the acidity of the stomach contents was profoundly reduced. Introducing 20 cc. of 0.34 N hydrochloric acid into the stomach evoked an even more striking

The occurrence of this phenomenon, clinically, is shown in Figure 16. The same ulcerous patient described earlier was examined during a period of considerable conflict and

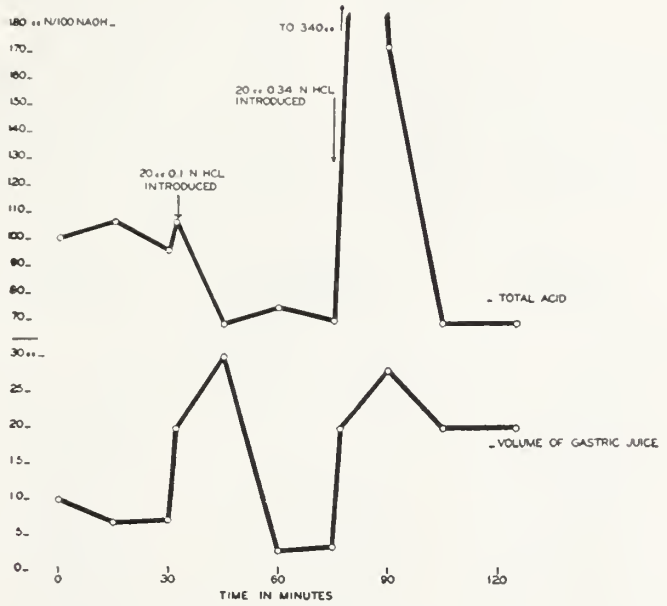

FIG. 15. ACCELERATION OF MUCOUS SECRETION AND INHIBITION OF PARIETAL SECRETION IN RESPONSE TO THE INTRODUCTION OF STRONG ACID INTO THE CAVITY OF THE STOMACH

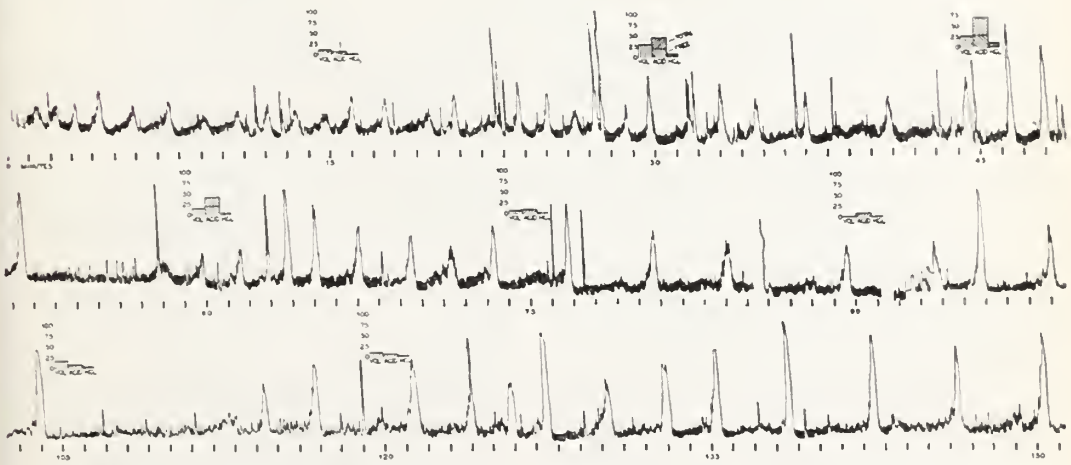

FIG. 16. INCREASED GASTRIC MOTOR ACTIVITY AND ACID SECRETION DURING STRESS WITH SUDDEN DECREASE IN ACIDITY FOLLOWING A PHASE OF HYPERSECRETION

elaboration of mucus, which within 15 minutes reduced by one-half the molar concentration of the acid. By 30 minutes the gastric acidity had returned to its former level.

troublesome epigastric pain a few days after his wife, with contempt for his earning power, took a job. During the first part of the experiment, not only was motor activity accelerated,

but also acid values were high. After they had climbed to a peak there was an obvious elaboration of mucus, associated with a decline in the titratable acid and apparently an actual decline in the production of HCl (Figure 16).

MODIFICATION OF THE EFFECT OF FOOD

The profound changes in gastric function which have been demonstrated to occur as part of an individual's reaction to problems and threats in his social setting may modify greatly the usually expected effects of differing diets on the accelerated function. The color of the mucosa was 60. Titratable free acid of the undigested material was 4. The pattern of contractions was different from that recorded at any time in the fasting stomach. The waves came in groups of 3–5, the earliest waves in the group being small, and each subsequent one higher, until they reached a size of about one-fourth that of the usual recorded vigorous contraction. Occasionally there occurred a short period of quiescence, followed by a similar group of waves. A

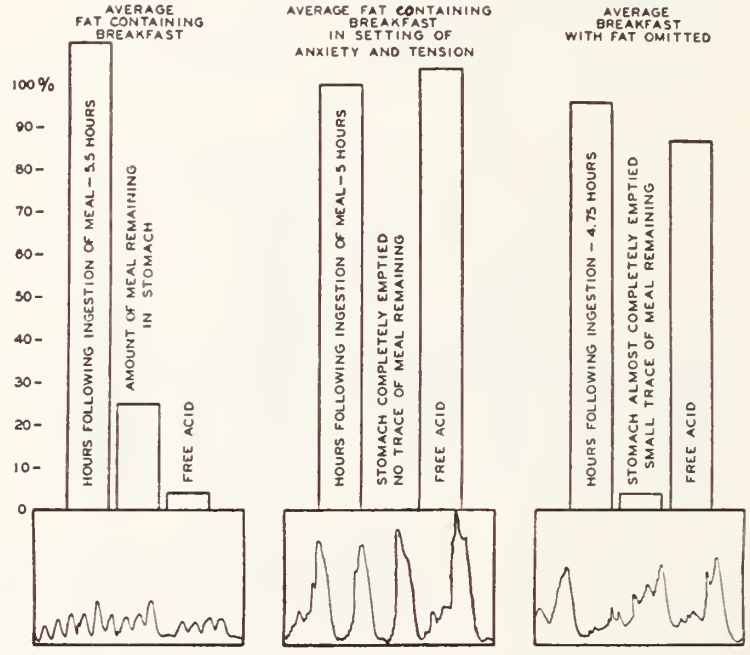

FIG. 17. DURATION OF GASTRIC DIGESTION UNDER VARIOUS CIRCUMSTANCES. MOTILITY PATTERN PREVAILING AT THE TIME THE STOMACH WAS EXAMINED IS REPRESENTED IN THE LOWER FRAMES

gastric motor activity and emptying time. Such a phenomenon is shown graphically in Figure 17.

At 6:30 A.M. the subject ate breakfast, which consisted of 2 eggs, scrambled in butter, 1 slice of buttered bread, 1 pint of milk, and 5 cups of weak coffee.

At noon, 5½ hours later, the process of digestion was not completed, 300 cc. of greasy, very fluid, yellowish gruel, approximately 25 per cent of the bulk of the meal being recovered. The stomach was not in a state of sample of this tracing is reproduced in Figure 17.

As a rule, under circumstances of relative security and contentment, the average breakfast was emptied from the stomach in 6 hours.

When the breakfast described above was eaten without butter or milk and with boiled eggs, the stomach was found to be entirely empty of food four and three-quarters hours after its ingestion. The organ was still intensely active, however. The mucosa was hyperaemic and engorged. Free acid was

88, and tall waves of contraction were occurring (see Figure 17).

When the breakfast detailed in the first experiment was eaten with 100 gm. extra butter, 6 hours later 10 per cent of the meal still remained in the stomach. The mucosa was pale, 45–50. Free acid was 23. No contractions, except the familiar basal 3-a-minute waves, were taking place.

The average breakfast, which contained approximately 50 gm. of fat, was ingested each morning during 3 weeks of emotional conflict involving anxiety and resentment. He was disturbed over his economic state, because of having loaned money unwisely to an irresponsible person, over an administrative delay in raising his pay from the hospital, the rising cost of wartime living, and the prospect of assuming new financial burdens with the support of his grandchildren.

Throughout this period his stomach was found to be emptied entirely of his breakfast in 4–5 hours, although under circumstances of relative contentment complete emptying would not be expected for from 5–6 hours. Furthermore, despite the presence of fat in the meal, his mucosa was hyperaemic, acid values were high, and motility active.

On one occasion in the midst of this period, he was entrusted with an errand which was obviously designed to test his eligibility for promotion to a more responsible job in the laboratory. He was intensely eager to discharge his responsibility creditably, and in his anxiety was overactive, overtalkative, and perspired a good deal.

His stomach was examined 5 hours after ingestion of breakfast. The stomach was empty. The mucosa was red (85), turgid and engorged. Free acid was 104, and motility was unusually active (see Figure 17).

MODIFICATION OF EFFECTS OF DRUGS

Concerning the introduction of drugs into the stomach, it is fair to generalize that vaso-constrictor substances give rise to a diminution in gastric function while vaso-dilators cause hyperfunction in the stomach (11). Effects which accompany variations in the subject's emotional state were found to modify the pharmacologic action of various agents as they do the results of the absorption of protein and fat.

Benadryl: During a period of relative relaxation and security when the gastric mucosa was comparatively pale and non-turgid and when the contractile activity was not more than average, 50 mg. of benadryl were introduced into the stomach. Within 15 minutes a perceptible pallor of the mucosa had occurred, associated with a diminution in turgidity and a corresponding decrease in acid output. There was a sharp acceleration of mucus secretion, however, as measured by the viscosity of the samples as well as by their mucin content (see Figure 18). This experiment was repeated when the gastric mucosa was relatively engorged and the stomach overactive in terms of acid secretion and motility during the period when Tom was experiencing feelings of special anxiety associated with hostility and resentment on the day following his step-granddaughter's broken engagement. When benadryl was administered in these amounts during this prevailing state of gastric hyperactivity it exerted no detectable effects (see Figure 19). Intermediate results were obtained when benadryl was administered during moderate gastric hyperactivity following recent ingestion of a meal or during anxiety of a mild degree.

Comment: The administration of pyribenzamine and a posterior pituitary extract was followed by similar effects, namely, inhibition of gastric function when the stomach was in an average state of activity but no demonstrable effect when administered during a phase of gastric hyperfunction.

Urogastrone:

Urogastrone, like benadryl and the other drugs mentioned above, was capable of inducing gastric hypofunction when administered under suitable conditions of relaxation and security but when administered during a period of sustained resentment associated with

hyperaemia, hypermotility and hyperacidity in the stomach its effect was not recognizable. The contrast of findings is illustrated in Figure 20.

Szasz, Levin, Kirsner and Palmer (12) have made similar observations in the case of enterogastrone. They found that this agent which usually effected a decrease in gastric acidity was ineffective when administered to an angry, resentful subject.

action in which, during an emergency, the stomach and digestion can wait.

When it is associated with nausea and vomiting the pattern of gastric hypofunction seems to indicate a need for riddance, an effort to reject noxious experiences. Such a riddance pattern is often accompanied by diarrhea and may also be associated with efforts at shutting out noxae, for example, with constriction of the esophagus, difficulty

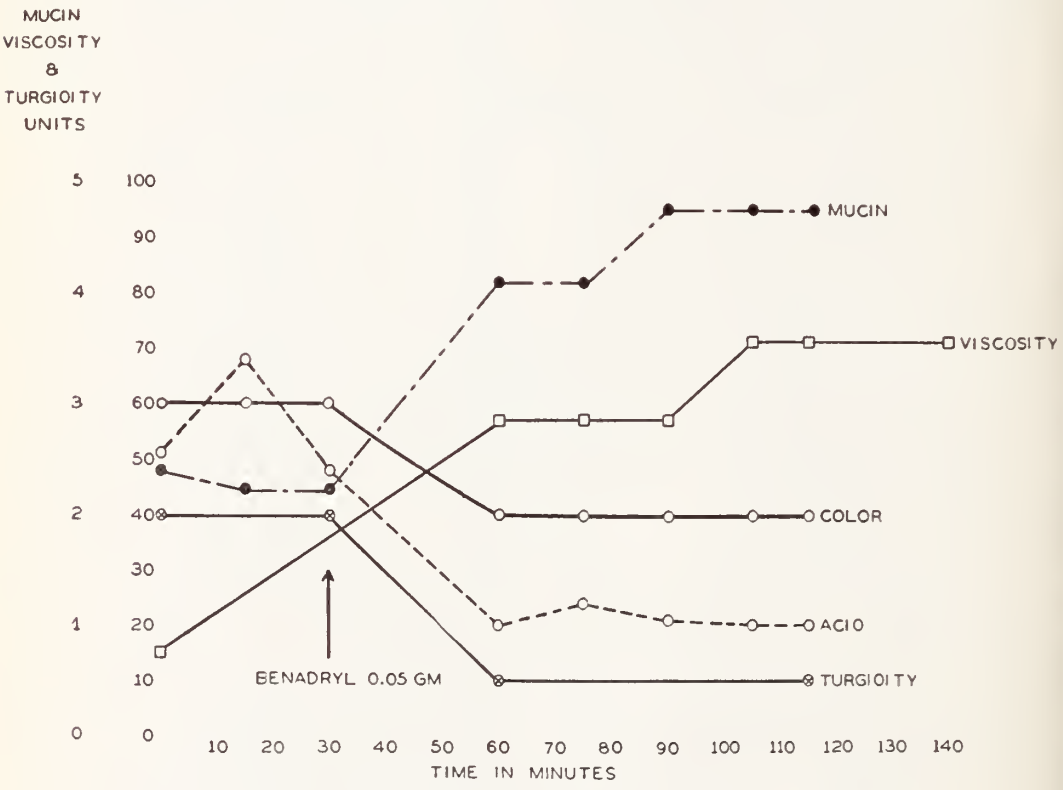

Fig. 18. Effect of Benadryl during Phase of Average Gastric Function

Biologic significance of patterns of disordered gastric function

It has been postulated elsewhere that the pattern of gastric hyperfunction, resembling as it does the state of the stomach during preparedness for food, may indicate a symbolic need for nourishment and sustenance at times of stress (13).

The pattern of hypofunction without nausea may represent, as Cannon has suggested, part of a general biologic pattern of mobilization for

in swallowing or refusal to eat. Often, however, instead of such an integrated pattern of rejection, fragments of the pattern existed by themselves. For example, certain patients displayed difficulty in bringing food to their mouths but no disturbance once it passed the teeth. Others ruminated the food and had difficulty in swallowing it but no disturbance once it was swallowed. Still others displayed only an esophageal disturbance with delay in passage of the bolus from hypopharynx to

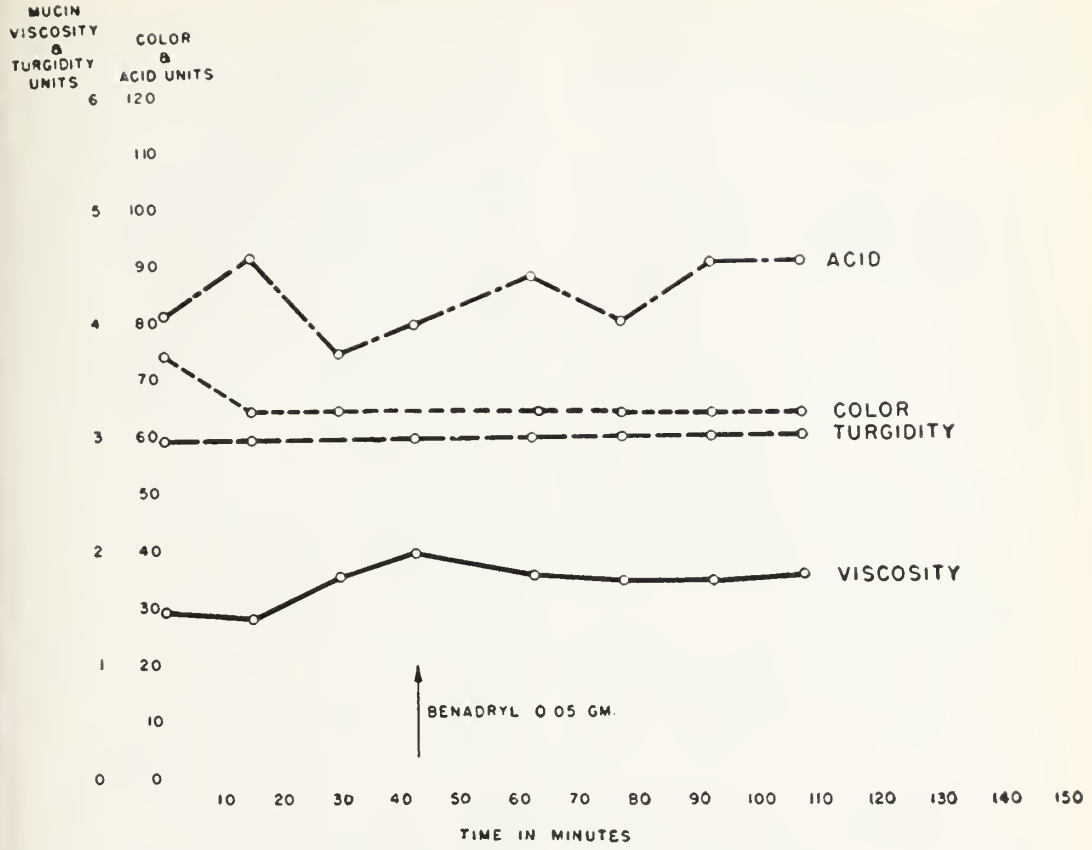

Fig. 19. Lack of Effect Following Administration of Benadryl during a Phase of Gastric Hyperactivity Related to Situational Stress

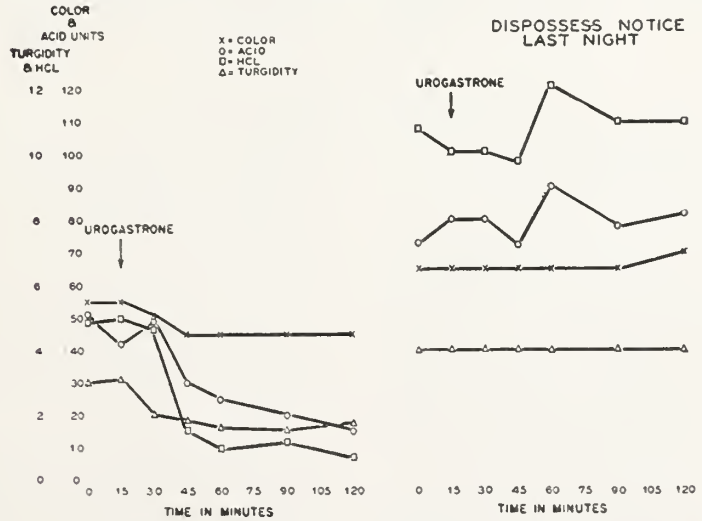

Fig. 20. Comparison of the Effect of the Gastric Inhibitor Urogastrone When Administered during Average Circumstances and When the Stomach was Markedly Hyperactive during Anxiety and Resentment following the Receipt of a Dispossess Notice

stomach. The existence of such fragmentary manifestations of biologic patterns of defense may indicate ambivalence or inner conflicts with incomplete direction of drives.

Summary and Conclusions

It is clear from these data that there occur in the stomach disturbances of function in response to threatening situations and that these disturbances may give rise to troublesome symptoms. In general, these patterns of disturbance are characterized either by overfunctioning of the stomach or underfunctioning of the organ. The same individual may display either under varying circumstances but one type of response may be characteristic for a given individual because of conditioning by an earlier experience productive of that particular pattern.

The degree of response in the stomach to stimuli arising out of situational stress was found to be great enough to modify or even cancel out the effects of the ingestion of various foods or drugs.

Gastric hyperactivity was found to be frequently associated with heartburn and epigastric pain of a gnawing quality, characteristically more intense during periods when the stomach was empty, and usually relieved by taking food, milk or alkalies. Gastric hypoactivity, on the other hand, was found to be accompanied by feelings of fullness in the epigastrium and nausea.

The principal difference between the emotional reactions accompanying gastric hyperfunction on the one hand, and hypofunction on the other, appears to be in whether or not the subject considers defeat at the hands of his adverse situation a 'fait accompli'. As Charles Darwin expressed it: "If we expect to suffer, we are anxious; if we have no hope of relief, we despair" (14). The individual whose stomach is hyperactive is physiologically prepared for food whether or not he has an appetite. He often feels angry in his need of being fed or cared for, but he is accepting his position vis-a-vis his situational threat and is doing something about it, preparing for either fight of flight. The individual whose stomach is hypoactive is not accepting the challenge of the situational threat. His associated nausea expresses his distaste for the situation.

Thus, life situations that give rise to anxiety and conflict may give rise to reactions that express the way in which the organism proposes to deal with the problem. It would be entirely appropriate for the gastrointestinal tract to participate in such a reaction since it is concerned with expressing and dealing with his most pressing needs for survival.

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Genetics and the Practice of Medicine*

By LAURENCE H. SNYDER, Sc.D.

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HUMAN progress has developed over the centuries along many streams, all flowing at varying rates towards that ultimate ocean, the health, happiness and prosperity of the human race. Rivers of art, culture, social science, government, economics and natural sciences have continued their unrelenting flow, occasionally temporarily dammed or diverted, but always finding new pathways and outlets. One of the strongest of these streams has been the mighty river of medicine. Starting in forgotten ages as a series of small rivulets, it has constantly and consistently flowed onward, pushing inexorably into many new channels while continuing to broaden and deepen its main course

From time to time important tributaries have joined the main stream, adding to its strength and its importance as one of the rivers of life. Other major rivers have from time to time sent out exploratory arms towards the stream of medical progress, which in many cases have anastomosed with it, often with the curious result of strengthening both streams. Such mutual anastomoses have been achieved between medicine and physics, chemistry, sociology, engineering and other channels of progress.

Among the newest of the streams of human progress is that swift-flowing branch of biological science, genetics, which, while retaining its source in the upper rivulets of biology has been strongly fed by the enthusiastic tapping of the productive springs of research and discovery along its own course. So strong and turbulent has the flow of genetics become, that it, too, has found itself able, and in fact required, to extend side-branches in the direction of other major streams. Mutually strengthening unions have been achieved with biochemistry, with physiology, with statistics, with population studies, and last, but not least, with the broad course of medicine itself. The anastomosis with medicine has been made through the wide reaches of preventive medicine and public health.

Tonight I should like to point out to you some of the ways in which this confluence of genetics and medicine may strengthen the powerful stream of medical progress. And, lest I run the risk of literally drowning you in metaphors, I shall speak now in more precise medical and genetic terms.

Medicine, and particularly public health aspects of medicine, have quite properly in the past directed their chief efforts towards the alleviation and control of unfavorable and dangerous agencies of the environment: infectious agents, trauma, malnutrition, occupational hazards, emotional stress, and others. Although occasional far-sighted physicians have seen and pointed out the possibilities of a genetic approach to the diagnosis and prevention of certain diseases and anomalies, there has been until recently but little factual material on which to base such hopes.

The last decade or two, however, have witnessed the very rapid development of human genetics, culminating in the birth of a new science, medical genetics. It is still a very young science, and has as yet barely scratched the surface of its potential assets, but it has already proved its indispensability as a powerful ally of medicine. The proof of this statement lies in the very practical applications of medical genetics which I shall shortly outline to you. Collateral evidence, however, is found in several other directions. First, those of us who are active in this field are being requested with increasing frequency to talk before medi-

* Mary Scott Newbold Lecture LX, the College of Physicians of Philadelphia, delivered at a joint meeting of the College and the Philadelphia County Medical Society, 13 October 1948.

cal groups. Second, the literature on medical genetics is becoming voluminous, and is constantly increasing. Third, a rising popular interest has resulted in the appearance of books and magazine articles on human genetics and its practical applications, and this has reached the point where the physician not acquainted with modern developments in the field may well find that his well-read patient has more knowledge of it than he himself has.

Fourth, courses in medical genetics are rapidly being incorporated into the medical curriculum. Fifteen years ago only two medical schools in this country included some material on genetics in other courses in the curriculum, and none had a specific course in the subject. Today four schools have required courses in medical genetics, nearly a dozen have elective courses, and forty-two schools present specific material on medical genetics in connection with clinical or didactic courses. Many schools have invited lecturers to present symposia or short courses on the subject, and it has been my privilege to participate in a number of these.

Fifth, there has just been formed a new North American organization, the American Society of Human Genetics, for the purpose of bringing into closer contact investigators in the many fields which involve human genetics. The new organization numbers among its large membership many medical men. It will publish a journal, to be called "Human and Medical Genetics", and should be a strong agency in encouraging research and education in this field.

The chief reason for all this interest in and attention to the new science of medical genetics is that the precision of our knowledge of the subject has now reached the point where specific practical applications are available and in use. These applications include (1) the solution of certain medical problems, such as maternal-fetal incompatibility, and certain medico-legal problems, such as the determination of non-paternity, on the basis of the inheritance of the various blood agglutinogens; (2) diagnosis, on the basis of genetic data, of conditions difficult to diagnose by other means; (3) treatment of affected persons, with appropriate therapy if there be any, based on the genetic diagnosis; (4) genetic prognosis for parents and prospective parents; (5) prevention of the appearance of specific diseases and anomalies through preventive measures based on genetic data.

The spectacular development and solution of the so-called "Rh problem" has thrown medical genetics into the forefront of modern medical progress. Although maternal-fetal incompatibility has important clinical aspects, it is primarily a problem of medical genetics, and is being solved largely through medico-genetic methods. Fortunately there are physicians interested in the problem who are themselves well trained in genetics, as well as interested geneticists whose primary training is in the methodology of human genetics.

The problem of maternal-fetal incompatibility is a specialized part of the larger problem of the occurrence and inheritance of human hemagglutinogens. Starting with the discovery in 1900 by Landsteiner of two such agglutinogens, A and B, and their combination into four blood groups, the problem has continually grown until we now know at least twenty-five hemagglutinogens in man, forming at least ten series, and capable of combination into more than two million "blood groups."

Each of these hemagglutinogens is inherited on a simple Mendelian basis, in such a way that a child never has a specific one of them unless at least one of the parents had it. If a child does possess one of these antigens, and one of the parents lacks it, the other parent must have had it. The various agglutinogens occur with diverse frequencies in different populations, and follow the laws of population genetics within populations, just as they follow the laws of Mendelian genetics within families.

These hemagglutinogens show varying degrees of antigenicity in man, and may or may not have natural antibodies in human individuals. Thus the laws of Mendelian genetics, population genetics, and immunology are

jointly responsible for the clinical implications of the blood groups.

Human hemagglutinogens thus far discovered appear to be of three sorts. First, there are those which are antigenic to man, but which are matched by normal antibodies, naturally occurring in the serum and other body fluids of individuals not possessing the antigens. Such agglutinogens are antigens A and B, and the variations of antigen A, now known as A^1, A^2, A^3, etc. Because of the reciprocal presence of natural antibodies against them, they are of the utmost importance in transfusions, even first transfusions.

TABLE 1

THE KNOWN HUMAN BLOOD GROUPS

BLOOD GROUP SYSTEMS	NUMBER OF PHENOTYPES
0, A^1, A^2, A^3, B, A^1B, A^2B, A^3B	8
Secretor, non-secretor	2
M, MS, N^1, N^2, N^1S, N^2S, MN^1, MN^2, MN^1S, MN^2S	10
P^1, P^2, P^1P^2, P−	4
C, C^u, C^w, c^v, c, CC^u, CC^w, Cc^v, Cc, C^uC^w, C^uc^v, C^uc, C^wc^v, C^wc, c^vc	15
D, D^u, d, DD^u, Dd, D^ud	6
E, Ee, e	3
Kell +, Kell−	2
Lewis +, Lewis−	2
Lutheran +, Lutheran−	2
Levay +, Levay−	2

$8 \times 2 \times 10 \times 4 \times 15 \times 6 \times 3 \times 2 \times 2 \times 2 \times 2 = 2{,}764{,}800$

The careful typing of donor and recipient prior to transfusion is now so commonplace as to need no further discussion.

Considering antigens A^1, A^2, A^3 and B, there are eight possible blood groups which may result from their combination (*Table 1*). Moreover, these antigens may be soluble only in alcohol, or they may also be soluble in water. Individuals having water-soluble antigens are known as "secretors," those not having them are "non-secretors." Since by means of special technics even individuals of group O may be classified in this way, each of the eight groups mentioned above may be either "secretor" or "non-secretor," thus making sixteen possible combinations.

The second kind of human hemagglutinogens includes those which have only immune antibodies, but which are very weakly, if at all, antigenic to man, so that the immune antibodies must be produced by injection of the antigen into animals. Such antigens are the agglutinogens M, N and P, and their various subtypes, discovered originally by Landsteiner and Levine in 1927, and presumably also antigen S, which modifies the M-N types, discovered by Walsh and Montgomery and studied by Sanger and Race. Here the antigens are of little or no clinical importance in transfusion, because of the absence of natural antibodies and the lack of antigenicity to man; but they are of great importance in medico-legal applications of the determination of disputed paternity, in a manner similar to the use of antigens A and B, and the secreting ability (*Table 2*).

TABLE 2

THE MAJOR LAWS PERTAINING TO THE MEDICO-LEGAL APPLICATIONS OF THE HUMAN BLOOD GROUPS

A. Laws for which there is adequate genetic evidence.

1. Hemagglutinogen A, B, M, N, P, C, c, D, or E cannot appear in a child unless it was present in one or both parents.
2. Water-soluble agglutinogen A or B cannot appear in a child unless one or both parents had the water-soluble agglutinogen.
3. A parent of group O cannot produce a child of group AB.
4. A parent of group AB cannot produce a child of group O.
5. A parent of type M cannot produce a child of type N.
6. A parent of type N cannot produce a child of type M.

B. Law which probably holds, but for which there is as yet insufficient genetic evidence.

1. Agglutinogen C^u, C^w, c^v, D^u, d, e, Kell, Lewis, Lutheran or Levay cannot appear in a child unless it was present in one or both parents.

The various combinations of antigens M, N^1, N^2, and S make it possible to classify people into ten so-called M-N types (*Table 1*). Since each of the 16 types previously mentioned

could be any one of these 10, the total number of possible combinations is now 160. Likewise the combinations of P^1, P^2 and P negative make four classifications possible, and since any one of the 160 possibilities just mentioned could be any one of these four P types, the total becomes 640 (see *Table 1*).

The third kind of human hemagglutinogen is made up of those antigens which, like the second kind, have only immune antibodies, but which, unlike the second kind, are, at least on occasion, highly antigenic to man. In such instances, immune antibodies are produced by transfusion, either intentional transfusion as a therapeutic measure, or unintentional transfusion such as sometimes takes place from an embryo to its mother.

At least 14 hemagglutinogens of this sort are known in man, headed by the antigen originally discovered by Landsteiner and Wiener, and named Rh. Although the original anti-Rh antibody was secured through immunization of animals with rhesus monkey blood, it is now known that Rh and similar antigens are antigenic to man, and that human immune serums are the best source of antibodies against them.

The fact that the original Rh antigen was antigenic to human individuals gave rise to two interesting applications. First, although the first transfusion of an Rh negative recipient with Rh positive blood could cause no immediate transfusion reaction, it could set up the production of antibodies. A later transfusion with similar blood might then result in a dangerous reaction in the recipient. Second, a "transfusion" may sometimes occur across the placenta from an embryo to its mother, causing the stimulation of antibody production in the mother against the Rh factor if it were present in the blood of the embryo and lacking in that of the mother. The presence of antibodies in the mother's blood might then be dangerous to a subsequent Rh positive fetus. This is, of course, the explanation of hemolytic disease of the new-born (Levine, Katzen and Burnham 1941).

The discovery that mothers of children with hemolytic disease frequently had antibodies demonstrable in their serums led to the further discovery that such mothers did not always produce identical antibodies, indicating that various antigens might be concerned with immunization. New hemagglutinogens discovered in this way by Wiener were named as varieties of Rh, the original Rh being named Rh_0, while others were called rh′, rh″, Rh_1, Rh_2, etc. Finally Levine discovered in this way an antibody which identified an antigen which was reciprocally related to rh′ much as N is to M. He called it, appropriately enough, Hr.

All these Rh and Hr antigens were found to be inherited by a child directly from one or both parents, so that the clinical picture is the direct result of a genetic situation which provides the proper setting for immunization. Moreover, these antigens could be added to the armamentarium for medico-legal applications involving disputed paternity.

In addition to active work by American investigators, British workers were participating in the researches on maternal-fetal incompatibility. Fisher, noting the reciprocal relationship of Levine's Hr to Wiener's rh′, suggested that the Hr factor was only one of a series of such factors, and could be called hr′, genetically allelic to rh′. He predicted that Rh_0 and rh″ would be found to have similar alleles, which could be called Hr_0 and hr″.

Finding that the use of the terms Rh and Hr with various subscripts and superscripts was becoming cumbersome, Fisher and Race suggested a simplified nomenclature, as follows:

Wiener	Fisher - Race
rh′	C
Rh_o	D
rh″	E
hr′	c
Hr_o	d
hr″	e

Race and Fisher further postulated that C and c were alleles at a certain locus on a pair of human chromosomes, D and d were alleles at a closely adjacent locus, and E and e alleles at another closely linked locus. Wiener, on

the other hand, considers the Rh antigens to be produced by a series of alleles all at the same locus. For all practical medical and medico-legal purposes, the two hypotheses are the same in the results they give, and the question of which is correct is at present largely academic. In Table 1 I have used the CDE nomenclature, since it appeals to me as being somewhat clearer.

In addition to antigens C, c, D, d, E and e, the British workers have described several others in the series, three being alleles of C, and one being an allele of D. Reference to Table 1 will show that there are thus 15 possible combinations (Rh groups) in regard to C, 6 in regard to D, and 3 in regard to E, or 270 altogether. Since any one of the 640 groups formerly described could also be any one of these 270, there are 172,800 possible combinations, and the number of individually distinct blood groups is becoming exceedingly large.

Of all the Rh factors, only D (Rh_0) appears to initiate antibody production strongly enough and often enough to be of real clinical significance. This antigen is the cause of the antibody formation in almost all of the instances of hemolytic disease of the newborn and in almost all of the severe transfusion reactions.

Since the other antibodies, and their causative antigens, were discovered through clinical manifestations, they cannot be ignored from a clinical standpoint. They are, however, of far less significance than antigen D.

In recent years the British workers have described four new antigens discovered in this same way, which seem to be quite independent of each other and of the Rh series. Thus far these antigens have been named only for the person who produced the diagnostic antibodies. The new hemagglutinogens are the Kell antigen, the Lewis antigen, the Lutheran antigen, and the Levay antigen (cf. Race 1946, Callender and Race 1946). Since every person must be Kell positive or Kell negative, Lewis positive or Lewis negative, and so on, and since each such newly-discovered antigen thus doubles the previous number of groups, it may be seen from Table 1 that there are now known 2,764,800 possible distinct blood groups.

Of course some of the antigens are exceedingly rare in all populations, so that certain combinations of antigens will be so improbable as to be practically non-existent. Nevertheless all of the more than two million blood groups are potentially possible, and many of them exist with reasonable frequencies.

Extensions of the work on human hemagglutinogens involves research in active progress at present on the possibility of effects of immunization other than transfusion reactions and the classical symptoms of erythroblastosis: effects such as blackwater fever as a sequella of malaria, congenital anomalies, and mental deficiency (for bibliography of current research see Snyder 1947 and Snyder and Reinhart 1947). Problems such as these are capable of solution only through the application of the methods of medical genetics.

This brief sketch of the blood group problems indicates one phase of the very practical applications of genetics to medicine. Turning now to another phase, that of diagnosis, it may be pointed out that it is sometimes possible for an alert physician to make an otherwise debatable diagnosis by taking into account the family history of the patient. Examples of such diagnoses have been presented on numerous other occasions (cf. Macklin 1941, Snyder 1943, Muller, Little and Snyder 1947), but I shall present a new example here.

I recently had occasion to give a series of lectures in medical genetics to a picked group of army medical officers, in connection with a course in basic science. After returning to his post, one of the officers sent me an excellent example of the use of genetic data in diagnosis. A man 51 years of age was admitted to the post hospital with symptoms of extreme breathlessness. It was noted that his fingers were clubbed, and this combination of symptoms suggested severe cardiac disease. Extensive study, however, revealed no clear evidence of pathology.

On at least three previous occasions the patient had been diagnosed by other physicians

as having serious heart disease, and on two of these occasions he was refused lucrative employment following the diagnosis. Recalling his training in medical genetics, the army physician asked the patient if anyone else in his family had clubbed fingers. The man replied that his father had them, as did two of his own children. The correct diagnosis was then made, namely, that the patient had inherited clubbed fingers, and that after being told so often by doctors, on the basis of this trait, that he had serious heart disease, he had developed an almost incapacitating anxiety reaction.

Taking up briefly the applications of human heredity to genetic prognosis, it should be pointed out that such applications, also, have been presented on many previous occasions (cf. Snyder 1941, 1946a, 1946b, 1948, Macklin 1940), and the various steps and criteria to be used have been outlined. In cases where the anomaly is known to be the result of a dominant factor with full penetrance, the prognosis for children where one parent has the trait is one chance in two that any child will have the anomaly. If the character is recessive, and one child in a family already shows it, even though neither parent shows it, the chance that any future child will show it is one in four. For each of the major types of hereditary behavior a different prognosis must be made. It behooves the physician to be acquainted with the various kinds of hereditary transmission, and to know where to look for specific information on particular diseases and anomalies. A good compendium of such information is Gates 1946.

A final application to be briefly surveyed is that of prevention, that is, the institution of preventive measures in those relatives of an affected patient who show early pre-clinical signs of the patient's anomaly. An example from personal experience may be permitted. During my course in medical genetics presented to medical students, it is my custom to have the hospital staff demonstrate cases illustrating various genetic diseases and anomalies. On one occasion I called the hospital and requested a case of hemolytic icterus for my class the following week, if one should be available. I was assured that they would try to have one available.

This hospital was one which had an excellent hematological service, and saw many cases of this disease, in which, as you will recall, the clinical manifestations are jaundice and marked anemia, sometimes developing as an acute fatal hemoclastic crisis if permitted to remain untreated. The condition is due to the presence of a dominant hereditary factor, but this factor does not always produce the full gamut of symptoms at once. One or another of the laboratory stigmata is, however, always demonstrable on appropriate examination. These signs include a relatively high reticulocytosis for the degree of anemia involved, increased fragility of the erythrocytes in hypotonic solutions of NaCl, increased icterus index, microspherocytosis, and an enlarged spleen in which many erythrocytes are sequestered.

Where one or another of these stigmata is found, it is indication that the person may some day undergo what would ordinarily be a minor event, such as an infection or broken bone, but which in him may precipitate a hemoclastic crisis capable of resulting in death. Removal of the spleen as a preventive measure is indicated in such instances. It is valuable, then, to examine the relatives of a patient with clinical activity, in the search for the laboratory stigmata.

But to get back to my class and the demonstration I desired. About a year previous to my request, a man had been operated on for hemolytic icterus, and as we always did, we called in his family for examination. Two of his four sons showed the early pre-clinical signs of the disease, and were advised to have their spleens removed as a prophylactic measure. One agreed, and his spleen was successfully removed; the other refused.

The day before my class period, I was advised by the staff that a boy with severe hemolytic icterus in hemoclastic crisis was on

his way to the hospital, and would probably serve for presentation the next day. When the hour for the class arrived, however, no patient was available. It had been the boy who a year earlier had refused preventive splenectomy. He died shortly after admission. But he could have been saved by elective prophylactic surgery on purely genetic grounds.

In the short time at my disposal I have been able to touch on but a few of the highlights of the relationships of genetics to the practice of medicine. It is my hope that this discussion may help to bring out the actual and potential value of these relationships, and to stimulate further observation and research along these lines.

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Memoir of William Pepper (1874–1947)*

By ISAAC STARR

IN writing a memorial for Dr. William Pepper for the records of the College of Physicians, I realize that I have been preceded by many others. A memorial written by Dr. A. N. Richards was delivered at the Medical Convocation on March 6, 1948 and has been published in the Pennsylvania Gazette. Memorial Resolutions have also been adopted by the Trustees of both the University of Pennsylvania and the Free Library of Philadelphia. I also have had before me citations read when honorary degrees were conferred on Dr. Pepper by the University of Pennsylvania and by Temple University. This long list of tributes excuses me from a lengthy review of his life and works and permits a more personal account perhaps better fitted to record what manner of man he was.

I remember my first contact with Dr. Pepper very clearly indeed, for I visited him in 1916 seeking admission to the medical school. He was of unusually large size; slow and slightly awkward in movement. He was sitting at his desk with his coat off, completely relaxed and with a kindly smile. He told me that I had been well recommended by my professors at Princeton and that he would be glad to have me in the class; a statement which would mean more nowadays than it did then, when both limitation of the class and discrimination between qualified applicants were unknown.

Dr. Pepper was away in the Army during much of the time that I was an undergraduate, but after I joined the faculty, I heard him speak in public many times and it is interesting to analyze the reason for his effectiveness. He had no great flow of language, indeed his delivery was a little halting. There was nothing whatever of the orator about him, for he was a modest man utterly without pretense. But every audience was impressed at once with his complete sincerity; and his talks commanded respect because of his ability to get right to the heart of the matter in a minimum of words. And they were not without flashes of humor, as when he mentioned that he seldom had much trouble with the students, but, on one occasion, he had been forced to go bail to keep a group of his professors out of jail (the occasion, I hasten to add, as he did not, being when the Animal House Committee was arrested at the instigation of the Anti-vivisectionists in 1912).

It can hardly be said that I knew him well until I was considering the deanship, and from that time on our contacts were close. I spent several weeks with him, sitting beside his desk and watching him handle the routine business of the office; interviews with applicants, with students and with the faculty. In these he was sympathetic, kindly and considerate. No one went away with the feeling that he had been brushed off. And Dr. Pepper had mastered the difficult art of saying "No", when the occasion demanded it, without giving offense.

This innate kindliness and courtesy extended to his correspondence also. As an example, let me quote from two of his standard letters. That of rejection read:

"Dear Sir:

The Committee on Admissions has carefully considered your application to the School of Medicine, and it is my unpleasant duty to inform you that you were not selected to be among those who are to enter our next First Year Class.

Because of the many hundreds who apply for admission it is impossible to admit many whom we would like to have in the school.

It is with regret that I am obliged to tell you of this decision upon your application.

Yours very truly,"

* Read at the meeting of the College of Physicians of Philadelphia, 13 October 1948.

And the letter informing students that they were dropped for scholastic deficiencies concluded, "I am sorry to write you like this but it is one of the unpleasant duties that deans must do." Could bad news be broken more kindly or with less wasting of words?

When I decided to accept the deanship, Dr. Pepper took me to my first meeting of the Association of American Medical Colleges. It so happened that the Trustees were acting on my appointment while we were away at the meeting, and when the time came to introduce new deans, he presented me, not as a new dean, but as one in process of being born. Many times I have been reminded of this at subsequent meetings by deans of other schools who paused to express their affectionate regard for him, and to inquire for his health.

When the time came for me to take over the deanship, there were tears in his eyes, and I was at pains to assure him that his services to the University were as valuable as ever and by no means at an end. He was provided with a room a few doors from the Dean's Office, and his successor sought his advice on any and all occasions. And I think I can truthfully say that it was always followed. Certainly the precedent of many years that the dean is absent from his desk on the first day of the trout fishing season was regularly adhered to.

As time passed Dr. Pepper's attendance at his new office diminished until it was limited to a few hours on Friday, before he attended the Orchestra. At last he was free to indulge himself in his two great hobbies, trout fishing and birds. His last illness was fortunately brief; he was stricken after a tooth extraction and taken to the Hospital. There I visited him, as usual to secure advice on a problem concerning the students, but I found him too sick and did not press my question. He died about a week later, the necropsy showing a ruptured aorta and a dissecting aneurism.

I can best conclude by transcribing part of the minutes of the Executive Committee of the Faculty Council of the School of Medicine, meeting on January 5, 1948.

"Dr. William Pepper graduated from our Medical School in 1897, he became Assistant Professor of Clinical Pathology in 1907, and became Dean in 1912. At first he divided his time between the Dean's Office and his teaching duties, but after 1919, he devoted all his time to the Deanship, becoming, as he believed, the first full-time Dean in the United States. His deanship, lasting 33 years, was a period of great growth and advance in our medical school, and, at the time of his retirement, he was senior in point of service to all Deans of American Medical Schools.

"Dr. Pepper was characterized by complete integrity and great friendliness. There is no record of his ever having had a quarrel with anyone, a fact which probably makes him unique among deans. The faculty admired, and respected him; the students loved him and took their troubles to him, to find that their interests were his interests. As was said of him by the Dean of another medical school, 'When he came to dealing with issues he could stand like the Rock of Gibraltar, and how well he represented the traditions and ideals of the University of Pennsylvania School of Medicine'.

"After his retirement in 1945, long sought by him, but repeatedly postponed because of the war, Dr. Pepper was the oldest faculty member in length of service, in the entire University. During this period, as Dean Emeritus, he was constantly at the service of his successor with the wisdom of long experience. He also continued to serve on the Board of Trustees of the University.

"The influence of his life and character on the Medical School he so loved and on the thousands of medical students whom he chose, supervised and presented for their degrees will continue for years to come."

Memoir of John Herr Musser (1883–1947)*

By GEORGE MORRIS PIERSOL

THE invitation to present a memoir of the late Dr. John Herr Musser before this College was accepted with a sense of deep satisfaction. It gives me the opportunity to pay tribute to a lifelong friend and close associate, and also, to carry out a tradition established 36 years ago, when on November 6, 1912, my father was accorded the privilege of reading before this College, in this same hall, a memoir of his classmate and colleague the senior Dr. John Herr Musser (*Transactions of the College of Physicians of Philadelphia*, 3rd series, Volume 24, 1912). Thus does coincidence emphasize the friendship and esteem that has existed throughout two generations of Philadelphia physicians.

John Herr Musser, the subject of these remarks, was born in Philadelphia on June 9, 1883. He received his early education at the famous old William Penn Charter School of Philadelphia, his B.S. degree from the University of Pennsylvania in 1905 and in 1908, when he obtained his M.D. from the same institution, John Musser became the sixth member of his family in direct descent to enter the profession of medicine.

His earliest medical ancestor was Dr. Benjamin Musser of Berne, who along with other hardy Swiss Mennonites, in 1710 settled in that part of Pennsylvania now known as Lancaster. Three more generations of Mussers faithfully served the medical needs of that growing community. Dr. Musser's father however, upon graduation from the Medical School of the University of Pennsylvania in 1877 chose to remain in Philadelphia, where he became, not only a famous physician, but one of the great medical leaders of his day and a distinguished Professor of Clinical Medicine at Pennsylvania. He held this position for many years, including the period during which his son pursued his studies as a medical student in their common Alma Mater. With such a medical background it is not surprising that from his schooldays on, John Musser never even considered the possibility of entering upon any career other than medicine. The prominence which he later achieved as a physician and teacher bore testimony to the wisdom of his choice, and proved him to be a worthy successor to his medical forebears.

After his graduation from the School of Medicine John Musser served an interneship of six months at the University Hospital, followed by two years at the Pennsylvania Hospital. He then spent a short period of graduate study at the University of Amsterdam before entering upon the practice of medicine in Philadelphia with his father. This fortunate association was terminated by the untimely death of the latter in 1912. When the elder Dr. Musser realized that he was fatally ill, he expressed the wish that his son and the writer of this memoir associate themselves in the practice of medicine. Such an arrangement, willingly entered into, continued for two years with mutual satisfaction and served to cement a friendship that began in boyhood and lasted throughout life.

Early in Dr. Musser's career his ability as a physician won him a growing practice and well-deserved professional recognition. In 1912 he was appointed Visiting Physician to the Presbyterian Hospital of Philadelphia. Two years later he was given a similar position on the staff of the Philadelphia General Hospital.

Dr. Musser's activities in medical teaching at the University of Pennsylvania began with his appointment as Associate in Medicine on the faculty of the School of Medicine (1914). Within a few years, he was made an Assistant

* Read at the meeting of the College of Physicians of Philadelphia, November 3, 1948.

Professor of Medicine, and in 1920 was promoted to Associate Professor. During these years at the University of Pennsylvania he directed and reorganized teaching in the Out-Patient Medical Clinic of the University Hospital and in many other ways demonstrated his interest in undergraduate medical instruction. His devotion to his Alma Mater was recognized by his election to the Board of Trustees as an Alumni Representative, and by the award, in 1940, of the Alumni Award of Merit of the University of Pennsylvania School of Medicine. Few honors had come to him from which he derived greater satisfaction.

Dr. Musser's successful practice and academic activities were interrupted by World War I. He was one of the first Philadelphia physicians to enter the medical corps of the United States Army at that time. In May of 1917, he was ordered to active duty with the rank of First Lieutenant. He was sent to France as a member of the University of Pennsylvania Base Hospital #20 in the late winter of 1918. While with that organization, he not only earned his majority and became Chief of the Medical Service, but, as a member of shock and gas teams at the front, repeatedly proved his courage and ability. Unlike many of his associates his interest in military medicine did not end with the termination of hostilities. He re-entered the Medical Reserve Corps of the Army, took an active part in the training of that organization and in 1938 attained the rank of Colonel. Although essential duties prevented him from entering upon active military service in World War II, he was appointed by the Secretary of War to the Committee charged with the study of the reorganization of the Surgeon General's Office.

Upon being relieved from active duty with the Army in the spring of 1919, Dr. Musser returned to Philadelphia, where he again took up an active consultation and hospital practice in Internal Medicine and entered upon a more ambitious teaching program. At this time he added to his many existing obligations those of physician to the Howard Hospital of Philadelphia. During the next few years the ever increasing demands of private practice made such inroads upon Dr. Musser's time that he was given scant opportunity to devote himself to the academic, literary and research aspects of medicine in which lay his greatest interest. It is not surprising, therefore, that in 1924 he accepted the appointment as Professor of Medicine and Head of the Department of Medicine at Tulane University, School of Medicine, New Orleans, a position which he held until his death.

When John Musser, at the age of 41, assumed the first full time professorship in a clinical department at Tulane University, he found himself in a tradition-bound, Southern city where Internal Medicine, as he knew it, had never been practiced as an accepted specialty. He was confronted with difficulties, and at times opposition. That he surmounted these obstacles and was able to develop one of the best Departments of Medicine in this Country, is a tribute to John Musser's integrity, energy, enthusiasm, tact and determination. His genial personality and unselfishness, coupled with his keen clinical judgement and deep human interest soon won for him the loyal, whole-hearted support of his colleagues and students. The 23 years which Dr. Musser spent in New Orleans, during which he was able to devote his major energies to teaching, writing and research, proved the most scientifically productive period of his life, years which brought him much satisfaction and happiness.

In addition to being an outstanding clinician and an effective teacher, Dr. Musser was a public spirited citizen. His interest in the welfare of his adopted State found expression in his accomplishments in the field of Public Health. Between 1940–1942, he served as Director of the Louisiana State Board of Health. During this time he completely reorganized the public health administrative machinery of the State, a contribution for which he was publicly acclaimed by Governor Jones of Louisiana. For 14 years he served as

President of the New Orleans Tuberculosis Association. In recognition of his work in this field, the new unit for tuberculous patients at the Charity Hospital was named for him. In addition he was a Director of the Child Guidance Center and President of the New Orleans Institution for Mental Hygiene.

In spite of his varied interests, Dr. Musser was always engaged in literary activities. From 1914 to 1921 he was Assistant Editor of the American Journal of the Medical Sciences. He assumed full editorship of that venerable Journal from 1922 to 1924. A few years after going to New Orleans (1927) he became Editor of the New Orleans Medical and Surgical Journal, a responsibility which he carried until his death. For 15 years (1932 to 1947) he performed outstanding service as a member of the editorial board of the Archives of Internal Medicine. One of his first literary efforts was the revision of his father's well known textbook entitled, "Practical Treatise on Medical Diagnosis", which he edited through four editions. After rewriting two other medical texts he entered upon his major literary achievement, the preparation of his textbook, "Internal Medicine, Its Theory and Practice", published in 1932. The fourth edition of this widely accepted and popular work appeared in 1945 and the fifth edition was in preparation at the time of his death. Aside from formal texts Dr. Musser published over 150 medical articles. Although his earlier papers dealt with the physiology and pathology of the spleen, for the most part, his contributions were devoted to clinical subjects. One of his last papers entitled, "The Heart That Is Ageing", was presented before this College.

Throughout his entire medical career, Dr. Musser took an active part in the deliberations and problems of County and State Medical Societies, and particularly in the American Medical Association. In that organization he held many positions. He was a member of the Council on Medical Education and Hospitals from 1934 on. He was vice-president and later Chairman of the Section on Pharmacology and Therapeutics of the American Medical Association in 1933 and 1934. From 1937 to 1938, he served as Chairman of the Section on the Practice of Medicine. In 1928 he was a member of the House of Delegates of the American Medical Association. Dr. Musser's name appeared upon the rolls of many scientific societies of major importance. Among these should be mentioned the College of Physicians of Philadelphia, to which he was elected in 1915. His interest in the affairs of this College was recognized when he became an elected councilor in 1923, an office which he held until 1926.

He took an active part in such distinguished groups as the Association of American Physicians, the American Society of Clinical Investigation, the American Clinical and Climatological Society, the Association for Research in Nervous and Mental Diseases, the Society of Internal Medicine of the Asociación Médica Argentina, Buenos Aires, of which he was a foreign corresponding member, as well as several intimate, inter-urban clinical and research groups and the American College of Physicians.

To no organization did John Musser give greater allegiance than to the last named. Elected a fellow in 1920, he served on the Board of Regents from 1926 to 1936 and was elected President of the American College of Physicians in 1929. In these several capacities he played an important part in the reorganization and development of the American College. In recognition of his years of devoted service the College bestowed upon him in 1947, its greatest honor, a Mastership.

Dr. Musser was instrumental in the formation of the original American Board of Internal Medicine, serving on this Board as a nominee from the Section of the Practice of Medicine of the American Medical Association, from the Board's inception until the expiration of his third term on July 1, 1935. As a member of this Board, John Musser made a significant contribution to the advancement of internal medicine in this country. A fellow member of

that Board has well said, "In no other capacity did the fine statesmanly qualities of John Musser stand in better stead than in the organization and early operation of the American Board of Internal Medicine."

The mere recital of professional success and scientific accomplishments fails to take a true measure of John Musser, the man. It was his even, cheerful disposition and personal charm that so endeared him to all whose privilege it was to know him and work with him. His forthright honesty and tempered judgement inspired confidence which impelled patients, colleagues and students alike to seek his counsel. In dealing with those who enjoyed his friendship, he exhibited an unselfish personal interest which all too often imposed upon his time and energy exactions which he could ill afford. Habitual, patient tolerance and unfailing good humor were not manifestations of weakness. They cloaked dogged determination of purpose and uncompromising courage that stood him in good stead when confronted by serious crises. The strength of his character was never more apparent than during his later years when grave disabilities imposed irksome restrictions upon his full and busy life. To his incapacity during those years was added the burden of family illness and the tragic death of his only son. In spite of physical handicaps and sorrow, the stout spirit of John Musser never faltered. Until the time of his death at his home in New Orleans on September 5, 1947, he retained his interest and pursued his daily tasks, within the limits of his failing strength, with uncomplaining courage.

The only members of Dr. Musser's immediate family to survive him are his widow, the former Marguerite Hopkinson of Philadelphia, his daughter, Mrs. Thomas L. Avengo, four grandchildren and his sister, Mrs. Richard M. Pearce.

John Musser, fearless, considerate gentleman and loyal friend, will be long remembered as an outstanding clinical teacher and scholarly writer who exerted a leading influence on American Medicine.

Catalogue of the Mütter Museum of the College of Physicians of Philadelphia

Compiled by ELLA N. WADE, *Curator*

PART II*

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Section 2

E. ABNORMALITIES

E. 1. a. Single Acquired

Skeleton

—female, with contracted thorax as a result of tight lacing. 1145.45.

* Part I was published in the *Transactions & Studies of the College of Physicians of Philadelphia* 15: 74–89, June, 1947; Part II. 1. Section 1, *ibid.* 15: 128–143, December, 1947. Reprints of the parts, as published, are obtainable from the Curator of the Mütter Museum.

Skull

—flattened occipital and frontal region caused by strapping the head to a board in infancy; Indian. 1008.40; 1006.141; 1006.200 to 1006.247 inclusive. A 7; A 8; A 79.

Vertebrae

—acquired deficiency of the wall of the vertebral canal. 1183.05. B.

Scapula

—epiphysis; artificial separation of. 1259.10. A 15.

Feet

—deformity of the feet of Chinese women due to bandaging. 8429; 8429.5 (M); 8429.6 (M); 8430 (M); 8432 (M); 8433 (M); 8434 (M). A 95.

E. 1. b. Single Congenital

Skull

—brachycephalic; skull of a lunatic. 1167.20. B.
—deformed; of male skeleton. 1145.50.
—microcephalic. 1006.037; 1006.052; 13500 (M). B 4.
—scaphocephalic. 1006.111. B 4.
—calvarium
  —atrophy. 17831.16.
  —bone translucent in deep Pacchionian depressions. 1167.30. B.
—facial bones; massive division. 1008.68. A 14.
—foramina; large parietal. 1006.110. B 4.
—malar bone; fissure in temporal side of frontal process. 1006.20. B.
—mandible
  —at obtuse angle; skull of a Digger Indian. 1167.00. A 6.
  —abnormally forward. 1008.61, C-79; dense. 1023.429, C-59. A 14.
  —massive. 1171.60; 1170.70; 1172.11. B; A 7.
—maxilla; hypoplasia. 1008.46. A 14.
—nasal septum, deflected. 1172.00. A 15.
—palate flattened; extremely large foramen magnum. 1008.79. A 14.
—processes
  —condyloid of the left side articulates with the squamous portion of the temporal bone and partly on the great wing of the sphenoid instead of the mandibular fossa. 1008.64, C-363-364-365. A 14.
  —paramastoid; articulates with the transverse process of the axis. 1183.00. A.
  —styloid; excessively long. 1006.107. B 4.
—sinus, maxillary; abnormal opening into. 1023.313. A 14.
—sutures
  —frontal; persistent. 1006.010; 1006.070; 1006.076; 1006.117; 1006.134; 1007.08; 1008.42; 1006.48; 1008.52. B 4; A 14.
  —palatine; more than the usual seven sutures radiating from the media suture toward the inner spaces between the teeth. 1008.84, C-73. A 14.
  —premaxillary; non-union of two in median line in skull of a child. 1008.83, C-71–72. A 14.
—turbinate bone, enlarged. 1008.74. A 14.
—Wormian bone, large. 1165.00; 1165.01. B.
—teeth
  —hypoplasia; skull of a typical mouth breather. 1008.47. A 14.
  —rudimentary molars. 1023.356, C-349; 1023.415. A 14.
  —anomalous, in skull of boy age 12 years. 1006.019. B 4.
  —maleruption of
    —canine. 1008.46; 1008.77. A 14.
    —incisor. 1171.00; 1171.50. B.
    —molar. 1023.303, C-157; 1023.432, C-169.
—unerupted molar. 1023.386. A 14.
  —improper occlusion. 1008.58, C-82–86 1008.54. A 14.
  —impacted
    —canine. 1023.369, C-148; 1008.71; 1023.380, C-144–145; 1023.389, C-146. A 14.
    —incisor. 1008.59, C-151; 1023.383, C-140. A 14.
    —molar. 1008.63, C-81–95; 1008.755; 1008.80; 1008.82, C-154–155; 1023.30; 1023.301, C-158; 1023.305; 1023.312; 1023.420, C-159–160; 1023.421, C-336–337–421; 1023.423, C-168; 1023.424, C-167; 1023.427, C-161-162; 1023.428; 1023.431, C-156; 1023.434, C-165–166. A 14.

—from prehistoric mandible. 1023.357, C-334-335. A 14.
—supernumerary. 1023.371, C-152; 1171.00. A; A 14.
—rudimentary. 1023.433 C-339. A 14.

Sacrum

—absence of posterior wall of spinal canal. 1183.30. A 16.

Vertebral column

—spina bifida. 1184.00; 1184.05; 1184.10; 7016.00; 8763 (M). A 15; A 86.
—sac excised. 5204. A 37.
—vertebrae
—posterior arches
—deficiency of. 1183.10. A 15.
—fissure of. 1183.20. A 15.

Clavicle

—of male skeleton, age 47 years; articulates with first rib; areas of ossification of costal cartilage. 1145.15. B.

Scapula

—acromion
—epiphysis; non-union. 1245.00; with ligamentous union. 1247.20. B; A 15.
—indentation of epiphyseal line. 1259.05. A 15.
—short; does not overhang glenoid cavity to usual extent. 1259.00. A 15.

Arm

—atrophy. 8427 (M).
—forearm
—deformed, in fetus. 7043.00 A 18.
—humerus
—epiphysis; non-union, in a child. 1274.00; 1274.05. A 12.
—ulna
—epiphysis; depressed line at the junction. 1304.00. A.
—and radius; epiphysis; non-union in an adult. 1289.00. B
—hand
—malformation. 8419 (M); 8422 (M).
—and atrophy. 1339.00. B.
—fingers
—malformation. 8420 (M); 8423 (M).
—and atrophy. 1350.00. B.

Femur and tibia (also humerus)

—epiphysis; non-union in a man age 23 years. 1005.05, A, B, C. A 18.

Pelvis

—contracted
—outlet. 1365.33 (M).
—generally. 1365.01. A 11.
—obliquely. 1365.12 (14e); 1365.00; 1365.13; 1365.22 (M); 1365.29 (M); 1365.35 (9h); 1365.39 (M); Nägele's. 1365.26 (M); 1365.27 (M) (9f). B.
—transversely. 1365.07; 1365.08; 1365.38 (M); Robert's. 1365.28 (M) (9g). B.
—deformed. 17834.54. A 11.
—dwarf. 17834.41 (9k). A 11.
—flat. 1145.30; 17834.45 (9m); 1409.00. B 5; A 11.
—funnel-shaped. 17834.39 (9j). A 11.
—kyphotic. 1365.09; 1365.10; 1365.11; 1365.14; 17834.38 (M) (17a); 1365.15 (M). A 11.
—justo-minor. 17834.44 (9l). A 11.
—with forward angulation of lumbar vertebrae. 1365.37 (M) (9i).

Ear

—anomaly of the stapes. 1059.014. B 4.
—external auditory canal
—constriction of. 1100.246 B. A 45.
—dilatation of. 1100.246 C. A 45.

E. 1. c. Single Developmental

Skull

—sutures; coronal; deformity due to premature disappearance. 1006.038; 1006.064; 1006. 092; 1006.034; sutures at vertex obliterated; retreating forehead, prognatious jaws (skull of Negro idiot). 1167.10. B.

Vertebrae

—synostosis in female skeleton. 1145.35. B 5.

Ribs

—synostosis. 1224.00; 1224.12; 1229.00. A 15 A 16.

Sternum

—ossification of costal cartilage. 1214.00. A 15.

Tarsus and metatarsus

—synostosis. 1494.10. A.

E. 1. d. Single; other than congenital or developmental

Vertebral column

—curvature. 1145.00; 1145.55; 1145.60; 1145.65; 1192.00; 1192.10; 1192.15; 1192.20; 1192.25; 1192.30; 1192.40; 1192.50; with ankylosis. 1194.920; 1194.925; 1194.930; 1194.950. B; A 1, A 15.

Humerus

—curvature. 1270.00. A 48.

Elbow-joint

—deformity. 8604 (M); 8604 A (M).

Wrist

—deformity. 8756 (M).

Leg

—deformity. 8191.55 (M); 8191.85 (M); 8717 (M); 8715 (M). A 53.
  —and foot. 8727 (M); 8728 (M).
—femur
  —deformity. 1409.00. A 15.
    —of head. 1404.13; 1404.48. B; A 1.
      —and neck. 1404.16. B.
  —epiphysis; separation of. 1409.10; 1409.15; 1409.20. B; A 12.
—tibia
  —epiphysis; separation of. 1442.07; 1454.55; 1454.60; 1454.65; 1454.70. B. A 12.
—knee; deformity. 8191.90 (M); 8191.96 (M); 8201.00 (M); 8704 (M); 8705 (M). A 53.
—ankle; deformity. 8191.80.

Foot

—deformity. 8726 (M).

E. 2. a. Multiple, Congenital

Fetus

—hydrocephalic. 1090.451; 5210.06. A 96; A 154.

Skeleton

—fetal; hydrocephalic. 1145.72.

Skull

—deformity; intra - uterine hydrocephalus. 1150.10 (6g); 1150.15. A 18.
—hydrocephalic; male, age 29 years. 8767 (M) (18a).

Feet

—flatfoot from a Negro. 1470.50 (12b). A 86.
—talipes
  —calcaneovarus. 8523 (M).
  —calcaneus. 8590 (M); 8591 (M); 8592 (M); 8593 (M). A 12; A 19.
  —equinovarus. 8573 (M); 8574 (M); 8580 (M); 8582 (M); 1470.00. B.
  —equinus. 8571 (M); 8575 (M); 8577 (M); 8578 (M); 8579 (M); 8585 (M); 8586 (M). A 12.
  —valgus. 8545 (M); 8550 (M); 8551 (M); 8552 (M); 8555 (M); 8556 (M); 8557 (M). A 12.
  —varus. 1000.55; 8500.5 (M); 8501.5 (M); 8502 (M); 8502.5 (M); 8503 (M); 8503.5 (M); 8504 (M); 8504.5 (M); 8505 (M); 8505.5 (M); 8506 (M); 8606.5 (M); 8507.5 (M); 8508 (M); 8508.5 (M); 8509 (M); 8509.5 (M); 8510 (M); 8510.5 (M); 8511.5 (M); 8512 (M); 8512.5 (M); 8513 (M); 8513.5 (M); 8514 (M); 8514.5 (M); 8515 (M); 8515.5 (M); 8516 (M); 8517 (M); 8517.5 (M); 8518 (M); 8519 (M); 8521.5 (M); 8522 (M); 8525 (M); 8526 (M); 8527 (M); 8528 (M); 8529 (M); 8530 (M); 8531 (M); 8532 (M); 8533 (M); 8534 (M); 8536 (M); 8537 (M); 8538 (M); 8539 (M); 8540 (M); 8541 (M); 8542 (M); 8583 (M); 8706 (M). A 1; A 12; A 15; A 58.

Monsters

—anencephalic
  —fetus. 7015; 7046. A 58.
    —male. 7042. A 89.
    —female. 7041.5. A 18.
  —with spina bifida
    —skeleton. 7020; 7021; 1036, CCC. B 5; A 87.
    —fetus
      —female. 7041; 7042.10; 7042.15. A 88; A 90.
      —male. 7045. A 18.
—bicephalic. 7011 (M).
  —ischiopagus tripus. 7003 (M) (19a).

—cranioschisis with meningocele. 7083 (M); with encephalocele. 8765 (M).
—cephalothoracopagus; skeleton. 7010.00 (6i). A 94.
—double; Siamese Twins. 7000 (M) (6q; 24a; 26a).
—ethmocephalus. 7050 (M) (12p). A 89.
—gastroschisis; fetus. 17831.93. A 92.
—spina bifida and clubfoot; fetus
—with exstrophy of abdominal organs; absence of anus and genitals. 7044. A 91.
—with part of abdominal wall wanting and through the opening the intestines, omentum and kidneys protrude. 7047 (6h). A 91.

E. 2. b. Multiple, Pathological

Skeleton

—of a child; deformity due to hydrocephalus. 1145.70.
—dwarf; rachitic; female. 1145.75 (10a; 11a). A 75.
—giant; height 7 feet 6 inches; lateral curvature. 1145.00 (6r; 27). B.
—male; height 6 feet 5 inches; prominent thorax. 1145.05.

Skull

—deformity due to hydrocephalus. 1163.00; 1163.20; 1006.080. A 1; B 4.

Hand

—of 232 cm. giant (acromegaly). 8403 (M). A 99.
—and foot (acromegaly). 8402 (M).

F. Healed Surgical Lesions

Amputated

—arm. 8860 (M).
—forearm. 8861 (M); 1319; 1319.10. A 15; A 51.
—humerus; false joint excised. 1274.15. A 12.
—hand. 8872 (M). A 12.
—phalanges. 8871 (M). A 12.
—thumb. 6155 (M). A 15.
—leg
—at the ankle. 8865 (M). A 12.
—below the knee. 8866 (M); 8867 (M); 8868 (M); 8873 (M); 1454.20; 1454.50. B; A 12.
—half way between the ankle and knee. 8869 (M). A 12.
—lower third. 1454.40. B.
—below tubercle of tibia. 1454.00; 1354.35. A.
—femur, at the middle. 1409.05; 1404.36; 1404.37. A 12; A 15.
—tibia. 1449.42.
—upper third. 1454.10; 1454.30. A 15; A 51.
—knee. 6040.00. A 21.
—knee-joint; epiphyseal separation caused by plate boiler iron falling against leg, breaking down, demanding amputation. 1048.06. A 84.
—foot
—Chopart's. 8864.00 (M).
—and ankle. 8870 (M).
—at ankle. 8863 (M); 8862 (M); 1484. A 15.
—phalanges. 8871 (M). A 12.

Trephined

—skull. 17830.52.
—skulls (19) of the Mūniz Peruvian Collection illustrating primitive trephining in which three types of operation are employed. 1143 to 1143.19 inclusive (16a). B.

Bone graft

—osteo-periosteal, by subcutaneous method illustrated on superior maxilla of dogs.
—at end of
—211 days. 1123.10.
—213 days. 1123.15.
—247 days. 1123.20. A 97.

2. Systems of the Body

A. Blood-Vascular System

A. 1. Diseases and Local Lesions

Heart

—aneurism
—with hypertrophy of ventricle. 2031.00. A 15.
—of ventricle
—and ascending arch of the aorta. 2031.05. A 15.
—with destruction of the anterior chest wall. 2031.10. A 15.
—atheroma
—of aortic valves. 2058.00; 2058.05; 2058.15; 2058.20. A 15.
—of mitral valves. 2057.00. A 15.

—calcification
—of aortic valves. 2058.26.
—degeneration (granular)
—of tricuspid valve. 2082.561. A 104.
—endocarditis. 2050.00. A 105.
—hypertrophy. 2025.05; 2060.00; 2082.30. A 15.
—and adherent pericardium. 2004.00; 2025.10 (12c). A 88; A 101.
—with dilatation. 2025.00; 2030.00; 2082.06. A; A 15; A 104.
—with fatty degeneration. 2028.00. A 58.
—myocarditis. 2035.00. A 104.
—obstruction in aortic and mitral valves. 2082.757.
—pericarditis
—endocarditis and adhesions. 2050.05. A 102.
—plastic. 2003.00. A 100
—rupture (spontaneous). 2029.00 (12d); 2029.10 (12e). A 51; A 53.
—stenosis
—of aortic valves, with calcareous degeneration. 2058.25 (12f); 2058.10. A 48; A 22.
—tumor from mitral valve. 2036.00. A 15.

Arteries and *Veins*

—aneurism
—of anomalous vessels. 5160.00. A 8.
—of aorta
—abdominal. 2084.00; 2084.10. A; A 15.
—and atheroma. 2082.30. A 101.
—of arch. 2082.06; 8191.75 (M); 2082.40; 2082.50; 17832.16; 2082.55; 2082.60; 2082.65; 2082.70; 2082.75; 2082.80; 2083.00. A; A 15.
—with clot. 2082.66. A.
—and innominate artery. 2082.61. A 85.
—multiple. 2084.20. A 15.
—of brachial artery. 8830.00 (M).
—of carotid artery. 2086.00. A 63.
—of a minute cerebral artery. 2089.00. A 105.
—of femoral artery; section of a clot of a sacciform aneurism. 2095.25. B.
—of tibial artery. 2093.00. A 15.
—of leg (false). 2079.00. A 109.
—popliteal. 8191.97 (M). A 15.
—organized coagulum from sac of. 2095.30. A 15.
—and clot; cross-section. 2031.15. A 15.
—aneurismal clot. 2031.20; and sac. 2077.00. A; A 15.
—apoplexy; of pulmonary artery (portion of lung). 2105.00. A 58.
—atheroma
—of aorta. 2082.562; 2030.00; 2082.15. A 15; A 104.
—abdominal
—and iliac arteries. 2065.05. A 15.
—and calcareous degeneration. 2082.00. A 15.
—with dilatation. 2082.05; 2082.20. A 15.
—of the arch. 2050.10; 2082.10. A 104. A 108.
—of coronary artery. 2060.00 (6k). A 107.
—endarteritis of aorta. 2050.10; 2050.00. A 104; A 105.
—hemorrhoids. 2162.00; 3109.00. A 15.
—ligature of femoral vein; 12th day after ligature. 2153.00. A 109.
—thrombus; wound of dura mater. 5178.00. A 55.
—varicose veins
—of hand. 8840 (M).
—of leg. 8841 (M).

A. 2. Abnormalities

Heart

—of patient with congenital cyanosis. 2020.00 (6j). A 48.
—interventricular sinus. 2015.20. A.
—large opening between the right and left auricle. 2046.00. A 104.
—aortic arch absent; heart vertical; only one auricle and one ventricle. 1068.65.
—valves
—eustachian
—enlarged. 2015.00. A 103.
—fenestrated. 2015.10 A 15.
—pulmonary; composed of two leaflets. 2082.562.

Arteries

—aorta; congenital stenosis. 2065.13 (M). A 70.
—subclavian; anomalous origin. 2061.05 (20a). A 7.

—vertebral; arises from aorta between the left common carotid and subclavian. 2061.00. A 15.

A. 3. Injuries

Heart

—and aorta
—laceration; aorta nearly severed. 2023.00. A 15.

B. Blood-making and Blood-destroying Organs

B. 1. Diseases and Local Lesions

Spleen

—hypertrophied. 3605.00. A 37.

B. 2. Abnormalities

Spleen

—and stomach; anomaly. 3601.00.

C. Lymphatic System

C. 1. Diseases and Local Lesions

Elephantiasis; leg. 8400 (M); 8400.5 (M); 8401 (M). A 12; A 15.
Lymphosarcoma of unknown origin. 6300.00.

D. Nervous System

D. 1. Diseases and Local Lesions

Brain

—abscess (sud-dural) from caries of the middle ear. 5120.00. A 67.
—angiosarcoma. 5210.1 (2d). A 78.
—clot in left cerebral hemisphere from a case of hemiplegia. 5177.10. A 105.
—dura mater
—fibrous thickening. 5152.00.
—ossific deposit. 5151.00. A 15.
—sarcoma. 5215. A.
—tumor. 5152.2.
—encephalitis; portion of brain of infant age thirteen days. 5182.00. A 27.
—encephalocele. 1150.50. A 85.
—of epileptics. 5003.00. A 160.
—hemorrhage into left ventricle. 5177.00. A 101
—tumor. 5210.00; 5210.05; 5210.15; 5210.16.

Spinal Cord

—pachymeningitis. 5305.00.
—and meninges; softening. 5302.00. A 15.

Nerves

—of hand
—fibrous tumors on digitial branches of median nerve; thickening of median and ulnar nerves. 5410.00. A 7.
—median nerve
—neuritis from splintered bone from gunshot wound. 5408.00 (6u). A 8.
—sciatic and internal and external popliteal
—fibroma. 5410.01. A 37.

D. 2. Abnormalities

Brain

—of murderer. 5050 (2c). A 160.

D. 3. Injuries

Brain

—dura mater; wound. 5111.00; 5178.00. A 55; A 107.

Spinal Cord

—bullet wound. 6045.30. A 55.

Nerves

—cast of hands showing
—areas of anesthesia and analgesia and impaired sense of touch after accidental section of ulnar nerve. 5402. (M).
—anesthesia and impaired sense of touch after section of musculospiral and median nerves. 5402.10 (M).
—condition of anesthesia after section of median nerve. 5402.15 (6t) (M).
—areas of dysesthesia and causalgia. 5402.20 (M).
—areas of dysesthesia nineteen days after stretching median nerve. 5402.21 (M).
—lines of operation; median stretched. 5402.22 (M).

E. Digestive System

E. 1. Diseases and Local Lesions

Tongue, tonsils and *epiglottis*
—ulceration; gangrenous. 2407.00.

Submaxillary gland

—scirrhus cancer. 3575.00. A 15.

Tonsil

—sarcoma. 2417.05. A 22.
—round-cell. 2417.00. A 37.
—papilloma. 6450.10. A 37.

Esophagus

—cancer. 3016.00; 3016.05. A; A 22.
—rupture. 3005.00. A 22.
—stricture. 8808 (M).

Abdomen

—cancer; colloid. 3105.15. A 15.

Peritoneum

—cancer; encephaloid of subserous tissues of peritoneum and pleura. 6475.00 (12r). A 8.
—sarcoma; spindle-cell, of retroperitoneum. 6310.05. A 24.

Omentum

—malignant disease. 3205.5. A 37.

Stomach

—atrophy. 3058.00. A 22.
—cancer. 3065.00; 3069.11; 3069.12; 3069.40; 3069.56. A; A 20; A 107.
—of cardiac end. 8810 (M).
—colloid. 3070.00. A 115.
—and dilatation. 3069.57. A 37.
—and occlusion of pyloris. 3069.50. A 114.
—of pyloric end. 8809 (M); 8809.5 (M). B.
—of pylorus. 3069.20. A 105.
—scirrhus. 3069.00 (12h). A 113.
—carcinoma
—and hypertrophy. 3056.00. A 8.
—and colon (portion of)
—epithelioma; gastrocolic fistula. 3063.00 (22a). A 51.
—fibroid thickening. 3072.00 (12i). A 8.
—hemorrhage (Petechial) in ruga. 3054.00. A 55.
—and intestines
—gastro-enterostomy. 3037.00. A 37.
—apposition by decalcified bone plates; experimental surgery. 6032.2; 6032.5.
—perforation of the wall. 3059.10. A 15.
—poisoning by corrosive sublimate. 3039.00. A 15.
—polypus of pyloric end. 3067.00. A 101.
—sacculated. 3052.00. A 15.
—ulcer. 3059.00; 3059.05. A.

Intestines

—anastomosis; lateral. 3077.10. A 37.
—cancer. 3105.30. A 20.
—of cecum. 3105.20; 3105.25. A 15.
—of sigmoid flexure; resection; experimental surgery. 3077.50. A 37.
—and stricture. 3105.00. A 27.
—carcinoma
—of sigmoid flexure. 3105.35.
—cholera; injected to determine effect of disease on mucous membranes. 3090.00 to 3090.20 inclusive. A 48.
—colitis. 3087.00
—enterorrhaphy; rubber ring method with omental flap. 6032.9.
—enterostomy. 3077.45.
—hernia
—femoral. 3310.00; 8303.(M). A 15.
—invagination of ileum. 3327.00. A 127.
—cecum and ascending and transverse colon. 3329.00 (12l). A 128.
—inguinal. 3113.50; 8300 (M). A 15; A 37.
—strangulated. 3310.10; 8304 (M). A 15.
—double. 3311.15. A 125.
—indirect. 8301 (M). A 15.
—mesenteric. 3322.00 A 126.
—sac of hernia and omentum; removed in operation for strangulated hernia. 3309.00. A 122.
—umbilical; direct. 8302 (M). A 15.
—ileocolostomy; experimental surgery. 6032.8; 6032.4.
—jejuno - ileostomy; experimental surgery. 6032.3; 6032.6.
—obstruction in. 3110.00. A 120.
—peritonitis of colon from gunshot wound. 3076.05. A 55.
—polypi. 3107.00. B.
—from strangulated femoral hernia. 3113.00. A 37.
—slough; ten inches of large intestines passed per anus as slough. 3331.00. A 129.
—stricture of small intestines. 3103.10. A.
—tuberculous mesenteric. 3202.00.
—typhoid fever; lesions of. 3099.00; 3099.05; 3099.10. A 15.

—ulceration
—with adhesions on peritoneal surface; tubercle bacilli cultivated from ulcers postmortem. 6290.00. A 55.
—of colon. 3092.05; 3092.10; 6240.00. A 55; A 101.
—dysentery ulcers of ileum and colon. 3098.00. A 55.
—of peritoneal coat of large intestines; case of fibroid thickening of the stomach. 3092.00. A 8.

Appendix vermiformis

—gangrenous, showing enterolith; large portion of omentum resected. 3130.50 (6m). A 122.
—perforation. 3120.00. A 15.
—and gangrene. 3130.00 (6m). A 121.
—peritonitis. 3131.00. A 123.

Rectum

—artificial anus. 3077.80. A 15.
—cancer. 3105.40. A 117.
—stricture. 3105.12. A 20.
—malignant disease. 3205.00. A 37.
—proctectomy. 3077.20. A 37.
—stricture. 3105.10. A 20.
—tumor (villous). 3108.00. A 119.

Liver

—abscess. 3416.00; 3416.10; 17832.14. A 15; A 131.
—cancer. 3423.00; 3423.10. A 15; A 132.
—cirrhosis. 3410.00. A 20.
—syphilitic. 3409.00. A 40.
—degeneration (cellular)
—with hypertrophy of gall-bladder and gall stones. 3455 (6n); 3456.00. A 133.
—melanosis. 3422.00. A 111.

Gall-bladder

—originally contained a calculus. 3450.00. A 15.
—with gall stones. 4229.00. A 104.
—hypertrophied
—and perforated. 3460.00. A 15.
—ruptured. 3454.00; 3454.1. A; A 104.

Pancreas (see also *Glands of Internal Secretion*)

—scirrhus cancer. 3540.00. A 134.

(See also Part VIII. Lantern Slides on Duodenal Tube Drainage of the Biliary Tract. 1066-Misc., CCC. A 172.)

E. 2. Abnormalities

Stomach and *Spleen*

—anomaly. 3601.00.

Intestines

—small
—duodenum; imperforate; congenital; gall-bladder absent. 3074.00 (12j). A 116.
—enlarged longitudinal gland. 3093.00. A.
—large
—megacolon; congenital. 3084.00 (23a). A 118.
—mesenteric glands enlarged. 3225.00. A 15.

Rectum

—and anus
—pouch of rectum. 3075.00. A 15.
—imperforate. 3074.10. A 20.

E. 3. Injuries

Stomach

—wound. 6045 00.

Intestines

—portion; gunshot wound. 3076.00. A 15.
—rupture of colon from external violence. 3076.10 (12k). A 7.

F. Respiratory System

F. 1. Diseases and Local Lesions

Nose

—polypus. 2404. A 15.
—postnasal. 2404.05. A 22.

Larynx

—abscesses. 2506.05. A 15.
—cancer. 2531.05. A 20.
—edema, following gunshot wound. 2507.00. A 22.
—epithelioma; tracheotomy. 2503.00 (12g). A 22.
—and epiglottis
—ulceration. 2509.10. A 15.
—ossification of thyroid and cricoid cartilages. 2505.10. A 106.
—and pharynx
—tumor. 2516.00.
—stricture
—syphilitic; laryngotomy. 2503.20. A 22.

—and tongue
—encephaloid cancer. 2531.00. A 22.
—tuberculosis. 2511.30 (21a). A 22.
—and trachea
—bronchi, lung and esophagus
—abscess of trachea; edema of glottis. 2506.00. A 15.
—diphtheritic membranes of croup. 2508.00. A 15.
—pneumonia from mustard gas; mucosa covered by dirty brown exudate. 2506.10. A 55.
—and roots of bronchi; exudate from gassing. 2506.15. A 55.
—stricture of larynx; tracheotomy; tuberculous laryngitis. 2503.10. A 22.
—and thyroid gland
—tumor. 2503.05. A 20.
—ulceration. 2509.00. A 15.
—syphilitic. 2510.00. A 22.
—of tracheal rings. 2509.40. A 27.
—tuberculous. 2511.10. A 22.
—of larynx; necrosis of right arytenoid cartilage; multiple enchondromata of tracheal rings. 2511.00. A 22.
—tracheotomy. 2503.30. A 22.
—tuberculosis. 2520.00; 2511.40; 2520.10. A 22; A 24.
—tumor. 2516.05. A 8.
—ulceration. 2509.20; 2509.30; 2509.31; 2509.50. A 15; A 22; A 101.
—syphilitic. 2510.10. A 22.
—tracheotomy. 2509.32. A 22.
—tuberculous. 2509.60; 2509.80; 2509.70. A 22; A 110.
—follicular, from a case of tuberculosis. 2511.20. A 22.

Trachea

—tracheotomy. 2503.06. A 20.

Lungs

—adhesions (pleuritis). 2506.00. A 101.
—anthrocosis. 2628.00. A 15.
—bronchopneumonia; mustard gas poisoning. 2623.00; 2623.10. A 55.
—cancer. 2642.00. A 105.
—cavity. 2636.10.
—from case of phthisis. 2636.00. A 51.
—collapsed; gunshot wound. 2620.00. A 55.
—with pyoneumothorax and gas bacillus infection. 2621.00. A 55.
—melanosis. 2638.00. A 111.
—peribronchitis; mustard gas poisoning. 2623.05. A 55.
—tubercle. 2633.10. A 15.
—abscess cavities. 2633.00.
—degenerated; from a case of fibroid thickening of stomach. 2633.20.

(For Obstruction in Bronchus see also Part VIII. Lantern Slides. 17832.86. A 112.)

F. 2. Abnormalities

Larynx

—false membrane. 2501.00. A 15.

Trachea and *Bronchi*

—enlarged bronchial gland. 2550.00. A 15.

F. 3. Injuries

Trachea

—foreign bodies. 2504.00; 2504.10; 2504.20 (61). A; A 15; A 24.

G. Urogenital System

G. 1. a. Diseases and Local Lesions of Urinary Organs

Kidney

—absorption from urethral stricture. 4015.00. A 15.
—calculus in pelvis. 4332.00; 4332.10; 4332.20; 4332.30; 4332.40; 4332.50. A 15; A 105.
—cancer. 4357.00 (60); 4357.10. A 105; A 139.
—cystic. 4339.00; 4339.30; 4339.38. A 15; A 130.
—and contracted. 4339.20. A 105.
—with calculi from a case of cystoma of liver and kidney. 4339.35 (25a). A 37.
—with phosphate calculi. 4339.40. A 58.
—embolism from patient who had ulcerative endocarditis. 4340.00. A 105.
—enlarged pelvis. 4375.00. A 15.
—fatty. 4329.00. A 136.
—hydronephrosis. 4334.00. A 46.
—laparotomy. 4334.10. A 139.
—nephritis
—acute. 4321.00. A 138.
—granular. 4320.00. A 104.
—interstitial (chronic). 4322.00.
—parenchymatous (suppurative). 4324.00. A 15.

—pathological conditions in pelvis. 10007 (Cr.). B 4.
—pyelonephritis. 4324.10; 4324.20; 4324.30. A 15.
—tuberculous. 4326.00. A 24.
—ulceration (scrofulous). 4324.50; 4335.00. A 15.
—and ureters
—distention of ureter which is larger than the kidney. 4346.00. A.
—bladder and penis
—cystic and contracted kidney, hypertrophied bladder and urethral false passage. 4020.00. A 104.

Bladder

—cystitis; hemorrhage from gunshot wound. 4215.10; 6045.20. A 55.
—fibroma. 4223.00. A 15.
—foreign body (watch guard) removed. 4228.00. A 104.
—hypertrophied. 4211.00; 4211.05.
—urethral stricture. 4020.10. A 104.
—kidneys
—and penis
—urethral stricture; sacculated, distended and ulcerated bladder; hyperdistention of ureters and acute nephritis. 4021.00. A 15.
—and penis
—urethral stricture. 4010.00. A 15.
—prostate and rectum
—urethral stricture, sacculated bladder and urethroperineal fistula. 4017.00. A 15.
—and prostate
—calcareous degeneration and hypertrophy. 4227.00. A 15.
—and penis; cystitis and gonorrhea. 4215.00. A 15.
—and rectum; papilloma of bladder. 4221.00. A 51.

G. 1. b. Diseases and Local Lesions of Male Reproductive Organs

Scrotum

—edema. 8789.00 (M).
—tumor. 8788.00 (M).

Testicle

—atrophy with vaginal hematocele. 4418.00; 4418.10. A 51.
—cancer. 4439.37. A 15.
—and cystic. 4439.35. A 15.
—scirrhus. 4439.00; 4439.10; 4439.20; 4439.40; 4439.50. A 15.
—cystic. 4446.05. A 15.
—traumatic origin. 4446.00. A 51.
—epididymis and tunica vaginalis
—hydrocele. 4456.00. A 15.
—fibroma. 4437.00; 4437.10. A.
—gumma; chronic syphilitic orchitis. 4441.00. A 140.
—orchitis. 4420.00; 4420.10. A 15; A 105.
—sarcoma. 4438.10; 4438.20; 4438.30; 4438.40; 4438.50; 4438.70; 4438.80. A 15.
—spindle-cell. 4438.60. A.
—tumor; multilocular cystic. 4437.20. A 122.
—and tunica; hydrocele (vaginal). 4456.10. A 105.
—varicocele. 4457.00. A 15.

Spermatic Cord

—cyst; double. 4453.00 A 7.
—hydrocele; encysted. 4447.00. A 140.
—lipoma. 4460.00 (20b); 4460.10. A 141.

Penis

—amputated. 4029.00. A 135.
—epithelioma. 4053.00. A 15.
—paraphimosis. 8789.00 (M).
—and testicle
—amputated by a man in an attack of delirium tremens. 4028.00 (20d).
—urethral stricture and false passage. 4026.00. A 15.

Prostate gland

—abscess. 4115.00. A 18.
—and bladder
—hypertrophy, 4110.00; 4110.10; 4110.15; 4110.20; 4110.25; 4110.30; 4110.35; 4110.40; 4110.45; 4110.50. A 15.
—carcinoma involving the bladder. 4100.00.
—prostatectomy. 4100.05. A 37.
—ulceration (tuberculous) of prostatic urethra. 4121.00.

G. 1. c. Diseases and Local Lesions of Female Reproductive Organs

Ovary

—cicatrix after ovariotomy
—six years after. 4680.10 (20f). A 53.

—sixteen years after. 4680.00 (20e 12o). A 7.
—cyst of. 4629.02; 6535.15 (20g); 4725.14; 4725.15; 4725.16; 4725.168; 4725.181; 4725.202; 4725.213; 4725.26; 4725.261; 4725.27; 4725.28; 4725.29. A 20; A 27; A 31; A 85; A 143; A 153.
—bilocular. 4725.12. A 27.
—contents. 4725.04. A 20; A 27.
—dermoid. 4730.05; 4730.10; 4730.12; 4730.13; 4730.20; 6539.20; 6538.00. A 46; A 117; A 142; A 143; A 146; A 150.
—and fibroid. 4730.00. A 144.
—hair from. 4630.14; 6539.00. A 142; A 27.
—teeth from. 6538.05. A 7.
—with hair. 6539.10. A 31.
—multilocular. 4725.175; 4725.18; 5725.185; 4725.186; 4725.191; A 20; A 142; A 150.
—multiple. 4725.169. A 20.
—parovarian. 4650.00. A 143.
—sarcoma in wall. 4746.00. A 117.
—unilocular. 4725.13; 4725.19; 6535.05. A 7; A 27.
—cystic. 4725.211; 4725.212; 4725.214. A 20.
—and fibroid. 4725.23; 4725.25. A 117.
—and diseased tubes. 4725.21. A 127.
—cystoma. 4725.235.
—fibroma; pediculated. 4745.05. A 116.
—oophoritis. 4659.143; 4659.144; 4659.145; 4659.1455; 4659.146; 4659.147; 4659.148; 4659.149; 4659.1495. A 151.
—sarcoma. 6310.50; 6310.49. A 7; A 117.
—spindle-celled. 4746.05. A 117.
—scirrhus. 4750.00. A 15.
—tuberculous. 4737.00. A 166.
—and tubes
—hydrosalpinx. 4656.00; 4656.20; 4656.30. A 31; A 96.
—double. 4656.10. A 117.
—pyosalpinx. 4659.1491. A 144.
—tumor. 4770.00; 4770.10. A 27.
—fibrocystic. 4725.172. A 143.
—simulating extra - uterine pregnancy. 6535.16. A 154.

Fallopian tube (see also *Diseases* of *ovary* and *uterus*)

—pyosalpinx. 4659.05; 4659.06; 4659.1; 4659.11; 4659.12; 4659.13; 4659.14; 4959.1415; 4659.16; 4659.17; 4659.18; 4659.19. A 150; A 117; A 151; A 37; A 143.
—with cyst of broad ligament. 4659.03.
—hysterectomy. 4659.00. A 143.
—with diseased ovary. 4659.141. A 151.
—tumor. 4661.00; 4835.00. A 15; A 152.
—also invading broad ligament. 4664.00.

Uterus

—abscess. 4612.30. A 145.
—adenocarcinoma; hysterectomy. 4634.2. A 144.
—adenoma. 4624.20. A 147.
—of cervix; hysterectomy. 4634.01. A 144.
—malignant. 4624.15. A 144.
—and appendages
—cancer. 4634.25. A 18.
—uterus and ovaries. 4634.45. A 20.
—cyst.
—of broad ligament. 4666.00; 4666.1; 4666.2. A 20.
—of ovary. 4625.02. A 27.
—cystic disease. 4625.01; 4625.03. A 18.
—cystic and fibroid ovaries. 4725.031. A 117.
—cystic myofibroma of broad ligament. 17834.66 (M). A 11.
—diseased. 4736.00. A.
—distention of Fallopian tube. 4658.00. A 101.
—dropsy of Fallopian tube. 4654.00.
—fibroma
—broad ligament. 4664.2; 6350.53. A 142.
—hematoma. 4627.46. A 117.
—of uterus. 4627.30; 4627.31; 4772.00. A 27; A 117.
—and ovaries. 4627.20; 4627.29; 4627.295. A 27.
—papilloma of broad ligament. 6450.01. A 20.
—peritonitis (granular). 4612.20. A 101.
—tuberculosis. 4660.00. A 117.
—cancer. 4634.00; 4634.10; 4634.12; 3077.35. A 18; A 27; A 117; A 51.
—endometrium thickened from case of membranous dysmenorrhea. 4613.00. A 146.
—epithelioma of cervix; hysterectomy. 4634.11; 4634.30. A 37; A 144.
—exudation; nodular. 17834.63 (M). A 11.
—fibroma. 4627.001 to 4627.009 inclusive; 4627.01; 4627.02; 4627.025; 4627.04; 4627.06 to 4627.10 inclusive; 4627.12; 4627.15;

4627.16; 4627.17; 4627.21; 4627.28; 4627.27; 4627.32; 4627.41; 4627.42; 4627.421; 4627.425; 4627.43; 4627.44; 4627.445; 4627.45; 4627.47; 4627.48; 4627.50 to 4627.55 inclusive; 4627.57; 4627.625; 4627.63; 4627.635; 4627.64 to 4627.68 inclusive; 6350.511; 6350.51; 6350.50; 6350.48; 6350.512; 4628.00; 4627.575; 4627.58; 4627.59; 4627.595; 4627.613; 4627.606; 4627.615; 4627.62; 4627.655 (12n). A 7; A 18; A 20; A 31; A 53; A 130; A 139; A 117; A 27; A 142; A 143; A 150; A 144; A 15.

—with calcareous degeneration. 4629.4. A 31.

—cystic. 4627.03; 4627.05; 4627.74. A 20; A 117; A 148.

—hysterectomy. 4627.13; 4627.14; 4627.69; 4627.70; 4628.1; 4627.13; 4627.56 (20c); 4627.71. A 27; A 142; A 144; A 143.

—multiple. 4627.60. A 149.

—and myoma with calcareous degeneration. 4627.11. A 117.

—obliteration of uterine cavity and obstruction of cervical canal. 4627.61 (6p). A 27.

—and placenta; fetus in situ. 4627.605. A 31.

—and polypus. 17832.64 (M). A 11.

—with pyosalpinx

—hysterectomy. 4627.19. A 144.

—remains of. 4627.18. A 20.

—sarcoma; fibrosarcoma. 6310.171. A 142.

—hematocele into connective tissues behind uterus. 17834.60 (M). A 11.

—hysterectomy. 4601.00; 4601.10; 4601.20; 4601.30; 4601.40. A 20; A 143; A 144.

—inflammation. 17843.61 (M); chronic. 4612.10. A 11; A 101.

—myoma. 4636.1; 4636.00; 4636.2; 4636.21; 17832.65 (M); 17832.66 (M); 17832.67 (M). A 11; A 117; A 142.

—myofibroma. 17834.68 (M). A 11.

—parametritis; puerperal. 17834.62 (M); chronic. 17834.65 (M). A 11.

—polypus. 4625.01; 4627.75. A 116.

—fibrous. 4626.00; 4627.40. A 7; A 27.

—sarcoma. 6310.17. A 142.

—round-cell. 4632.00. A 117.

—tumor. 4624.05; 4624.10; 4625.00. A 51.

—osseous. 4629.00. A 18.

Vagina

—fibroma. 6350.54. A 142.

Vulva

—and anus; fibroma. 4511.30. A.

—cancer; epithelial of clitoris. 4512.00. A 18.

—cyst of gland of Bartholin. 4506.00. A 20.

—fibroma. 4511.00; labium majus. 4511.25. A 15; A 139.

—pedunculated. 4511.10; 4511.20. A 15.

Mammary Gland (accessory organ) (see also Part IX. Microscopic Slides. 11119.00 to 11128.00 inclusive. A 173.)

—cancer. 4910.25; 4910.31. A 27; A 142.

—carcinoma. 4918.13. A 20.

—sarcoma; spindle-cell. 6310.19. A 37.

—scirrhus. 4918.11; 4918.12; 6470.11; 6470.10; 6470.09. A 7; A 20; A 37.

—tumor. 4910.01; 4910.05; 4910.10; 4910.12; 4910.15; 4910.20; 4910.30; 4910.35; 4910.40; 4910.45; 4910.48; 4910.50; 4910.52; 4910.54; 4910.57; 4910.58; 4910.60; 4910.62; 4910.64; 4910.65; 4910.67; 4910.68; 4910.69; 4910.50. A 15; A 18; A 20.

G. 1. d. Morbid Parturition

Uterus

—cervix severed during labor. 4850.00. A 133.

—cesarean section performed; skeleton of rachitic dwarf. 1145.75 (10a; 11a). A 75.

—fetus delivered by craniotomy. 4892.00 (6s). A 18.

—fibroma, complicating pregnancy. 4870.00. A 31.

—fibromyoma, complicating pregnancy. 4845.00. A 7.

—scirrhus. 4866.20.

Placenta

—retained. 4885.00. A 27.

Vulva and *rectum*

—recto-vaginal fistula. 4866.00; 4866.10; 4866.20. A; A 18.

Ovum and *membranes*

—myxomatous disease of chorion. 4800.00. A 15.

G. 2. a. Abnormalities of Urinary Organs

Kidney

—lobulated. 4302.00. A.

—single. 4300.05.

LIBRARY OF THE COLLEGE OF PHYSICIANS OF PHILADELPHIA

—and ureter; single kidney; congenital. 4300.00 (12m). A 51.

Bladder

—double; two of equal size united by contact of their walls. 4201.00. A 137.
—exstrophy; closure forming new perineal floor. 4200.00. A 37.

G. 2. b. Abnormalities of Male Reproductive Organs

Testicle

—cryptorchism. 4400.00. A 46.

Penis

—phimosis. 4031.00.

G. 2. c. Abnormalities of Female Reproductive Organs

Uterus

—anomalous uteri. 17832.58 (M); 17832.59 (M); 17832.60 (M); 17832.62 (M); 17832.63 (M). A 11.
—cervix elongated. 4617.00. A 27.
—inverted. 17834.68 (M). A 11.

G. 2. d. Abnormal Pregnancy

Abortion

—at four and one-half months; triplets. 4815.00; at three months. 4815.20. A 155; A 98.
—tubes, ovaries and uterus
  —removed ten days after abortion. 4815.10. A 117.
  —from patient suffering puerperal septicemia; removed two weeks after. 4815.5. A 117.

Extra-uterine pregnancy

—1090.008 (M); 1090.009 (M); 4835.01; 4835.06; 4835.08; 4835.30; 4835.37; 4835.41. A 117; A 144; A 158.
  —double. 4835.20 (12q). A 105.
  —ovaries and tubes. 4835.38. A 142.

Presentation

—fetus presents by shoulder and neck. 4897.00.

Tubal pregnancy

—4835.00. A 15.
—ruptured; fetus in abdomen. 4835.07. A 143.
—ruptured. 4835.11. A 143.
—unruptured of sixth week; fetus. 4835.12. A 146.

Tubo-ovarian pregnancy

—ruptured; uterus and appendages. 4835.39. A 117.

Umbilical cord

—with forty-six twists. 4825.00. A 156.
—with twenty-six twists. 4825.1. A 157.
—knotted in utero. 4825.2; 4825.3. A 24; A 27.

G. 3. a. Injuries to Urinary Organs

Kidney

—rupture. 4306.00. A 55.

Bladder

—cystic; through and through gunshot wound. 6045.20. A 55.

G. 3. b. Injuries to Male Reproductive Organs

Testicle

—driven into the inguinal canal; fatty degeneration and atrophy. 4405.00 (20h). A 26.

Penis

—and skin; bullet wound. 6045.14. A 55.

H. Special Sense-Organs

H. 1. Eye

H. 1. a. Diseases and Local Lesions

Eyeball

—cancer. 9264 (M). B.
—coloration in jaundice. 9217 (M). B.
—hydrophthalmos. 9259 (M). B.
—black pigmented spots. 9231 (M). B.
—polypus. 9262 (M). B.
  —in nasal fossa, pushing eye out of orbit. 9265 (M). B.
—sarcoma; melanotic. 6315.00. A 15.

—scaly covering. 9289 (M). B.
—tumor. 9263 (M). B.

Cornea

—abscess. 9240 (M); 9241 (M). B.
—circumcorneal injection. 9230 (M). B.
—collapse. 9258 (M). B.
—keratitis
—interstitial. 9234 (M). B.
—punctate; serous iritis. 9235 (M). B.
—suppurative; ulcer. 9326 (M). B.
—due to injury. 9282 (M). B.
—opacity. 9290 (M); 9291 (M). B.
—pannus. 9225 (M). B.
—senile degeneration. 9288 (M). B.
—staphyloma. 5610.00.
—conical propulsion. 9285 (M). B.
—dislocation of the lens (glaucomatous). 9254 (M). B.
—opaque. 9287 (M). B.
—ulcer; perforating. 9237 (M). B.

Sclera

—episcleritis. 9228 (M). B.

Choroid

—calcareous degeneration. 6030.10. A 165.
—melanosarcoma (section). 6315.5. A 165.
—tumor of membranes. 9283 (M). B.

Iris

—iritis. 9292 (M). B.
—syphilitic. 9293 (M). B.
—hernia. 9295 (M). B.
—perforation. 9294 (M). B.
—staphyloma. 9299 (M). B.
—synechia
—anterior. 9298 (M). B.
—posterior. 9296 (M); 9297 (M). B.

Pupil

—mydriasis. 9299.2 (M). B.
—myosis. 9299.1 (M). B.

Crystalline lens

—cataract
—anterior polar. 9243 (M). B.
—black. 9245 (M). B.
—capsular
—anterior. 9251 (M). B.
—posterior. 9252 (M). B.
—punctate. 9249 (M). B.
—pyramidal. 9253 (M). B.
—chalky. 9246 (M). B.
—hemorrhagic. 9256 (M). B.
—incipient. 9244 (M). B.
—morgagnian. 9250 (M). B.
—nuclear. 9247 (M). B.
—purulent. 9255 (M). B.
—stellate; incipient. 9248 (M). B.

Conjunctiva

—conjunctivitis
—catarrhal. 9219 (M). B.
—herpetic. 9220 (M). B.
—phlyctenular. 9218 (M). B.
—purulent. 9222 (M); 9223 (M); cornea ulcerated and collapsed. 9224 (M); 9229 (M). B.
—papilloma; malignant. 9232 (M). B.
—papules; opaline syphilitic. 9227 (M). B.
—pterygium. 9226 (M). B.

Lacrimal gland

—carcinoma of lacrimal duct causing exophthalmos. 9210 (M). B.
—epiphora; obstruction. 9209 (M). B.
—sarcoma. 6310.12 (28a).
—tumor of the duct with obstruction and blenorrhoea of sac. 9211 (M).
—abscess of sac. 9214 (M).
—fistula of sac. 9212 (M).

Anterior chamber

—dropsy. 9284 (M). B.
—pus. 9286 (M). B.

Vitreous humor

—hernia into anterior chamber. 9242 (M). B.

Eyelid

—abscess. 9213 (M). B.
—ankyloblepharon. 9266 (M). B.
—blepharitis, ciliaris. 9275 (M); 9276 (M). B.
—blepharoptosis. 9270 (M). B.
—ecchymosis with hyphemia. 9280 (M). B.
—ectropion. 9269 (M); 9271 (M); 9272 (M). B.
—enstrophe. 9273 (M). B.
—epicanthus. 9268 (M). B.
—gangrene. 9278 (M). B.

—pustules
—caused by inflammation. 9201 (M). B.
—malignant. 9277 (M). B.
—tumor
—chalazion (meibomian cyst). 9203 (M); 9204 (M); 9279 (M). B.
—fungoid cancerous. 9206 (M). B.
—melanotic. 9202 (M). B.
—polypoid of inner canthus. 9215 (M). B.
—ulceration
—cancerous. 9205 (M). B.
—indurated syphilitic. 9207 (M). B.
—and nose, involving the lacrimal sac. 9216 (M). B.
—verucca. 9281 (M). B.

Ciliary region

—cyclitis complicated with retinitis. 9260 (M). B.
—sarcoma; melanotic. 9233 (M). B.
—trichiasis. 9274 (M). B.

H. 1. b. Abnormalities of the Eye

Eye

—strabismus. 9257 (M); 9261 (M). B.

Eyelid

—epicanthus. 9268 (M). B.
—naevus; congenital. 9208 (M). B.

H. 1. c. Injuries to the Eye

Eyeball

—penetrated by splinter of wood. 9239 (M). B.

Cornea

—chip of iron imbedded. 9238 (M). B.

H. 2. Ear

H. 2. a. Diseases and Local Lesions

Tympanic membrance (from the Politzer Collection)

—adhesions; funnel-shaped, below the manubrium to the inner wall of the tympanic cavity. 1100.231. A 45.
—calcareous deposit. 1100.227; 1100.228; 1100.229; 1100.230. A 45.
—cicatrix upon anterior half. 1100.239. A 45.
—degeneration and adhesions. 1100.243. A 45.
—destruction almost complete; adhesions of tip of manubrium to promontory. 1100.234. A 45.
—manubrium detached. 1100.233. A 45.
—perforation. 1100.241; 1100.242; 1100.261. A 45.
—and ankylosis of the stapes. 1100.235. A 45.
—and adhesion between a cicatrix of the tympanic membrane and inner wall of tympanic cavity. 1100.240. A 45.
—and calcareous deposits. 1100.232; 1100.259; 1100.260; 1100.267. A 45.
—double. 1100.236; 1100.237. A 45.
—triple. 1100.238. A 45.

H. 2. b. Abnormalities of the Ear

Auditory canal

—congenital dilation. 1100.246. A 45.
—congenital constriction. 1100.246. A 45.
—styloid process with several prongs. 1100.246. A 45.

I. Muscles, Ligaments and Tendons

I. 1. Diseases and Local Lesions

Diaphragm

—cancer. 2725.00. A 105.

Achilles tendon

—repair after subcutaneous division to relieve talipes. 1724.00. A 15.

I. 2. Injuries

Tendon

—avulsion
—of finger. 1354.50. A 98.
—of foot; injury result of forcible extension; separation of calcaneo-astragaloid joint. 1720.50.
—of thumb. 1354.00; 1720.00. A 15.
—laceration as though caused by crushing force; sloughing of the foot. 6150. A 15.

J. Skin

J. 1. Diseases and Local Lesions

Cellulitis

—arm and hand. 6095.00. A 53.
—ankle and foot. 6095.10. A 15.

Skin in *Cerebral-spinal meningitis.* 5121.00 A 55.

Leprosy

—of foot. 6325.1. A 169.
—elephantiasis graecorum, from West Indies. 6005.00. A 164.
—hand of tuberculous leper. 6325.2 (6v). A 169.

J. 2. Abnormalities of Skin

Human horn

—6002 (M). 6002.10. A 163.

J. 3. Injuries to Skin

Wound

—6045.13. A 55.
—of skin and penis. 6045.14.
—of skin from bullet. 6045.12. A 55.

K. Glands of Internal Secretion

K. 1. Diseases and Local Lesions

Adrenal

—Addison's Disease. 3800.00 A 124.
—tuberculosis. 17832.15.

Pancreas (see E. 1. Digestive System)

Thyroid

—cystic 6533.00. A 22.
—and enlarged. 3900.15. A 37.
—goitre. 3900.10; 6550.10; 6550.15. A 15; A 122.
—and calcareous degeneration. 6550.05. A 15.
—hypertrophy. 3900.00; 6550.00; 6550.07. A 15; A107; A 37.

K. 2. Abnormalities

Pituitary (see E. 2. b. Multiple Pathological Specimens; giantism; acromegaly).

3. Tumors (see aso Diseases of Bones and of Systems of the Body)

Adenoma

—fibrochondromatous, from cervical region. 6390.20. A 171.
—of leg and foot. 8729.00 (M).

Cancer

—medullary of thigh. 6476 (12s). A 8.

Cancroid

—6511.00. A 15.

Cystic

—of nates of new-born child. 6532.00; 6532.10. A 133.
—of neck. 6531.00; congenital. 6531.10. A 15.
—sac of. 6530.00; 6530.10. A; A 15.
—of back. 6530.01. A 37.
—scalp. 6534.00; 6534.05; 6534.10; 6534.20; 6534.25. A 15.
—from submaxillary triangle. 6531.5. A 170.
—hydatid. 4800.10. A 27.

Dermoid

—from floor of mouth. 6538.60. A 109.

Enchondroma

—arm. 6390.10. A 15.
—hand. 6390.15. A 15.
—and thumb. 6390.00.
—thumb. 6390.05. A 15.

Encysted

—from shoulder. 6512.00. A 15.

Epithelioma

—fingers. 6480.10. A 15.
—foot. 6480.06; 6480.20. A; A 109.
—hand. 6480.01. A 51.
—jaw. 6480.25.
—lip. 6480.00; 6480.05. A 15.

Fibroma

—6350.00; 6350.30; 6350.60; 6350.65; 6350.70. A 15.
—with cavity. 6350.45.
—of ear. 6350.76. A 37.
—of jaw. 6350.55. A 15.
—lobulated. 6350.11; 6350.25; 6350.40. A 15.
—of neck. 6350.35. B.
—of scalp. 6350.75. A 15.
—of shoulder. 6350.42.

Fibroplastic

—of hip. 6350.15. A 15.

Fungous

—6513.00. A 15
—hematodes. 6310.35. A 15.
—of shoulder. 6310.36.

Lipoma

—of back. 6370.01; 6370.11. A 37; A 170.
—lobulated. 6370.30; 6370.40. A 15.
—of neck. 6370.50. A 15.
—of shoulder. 6370.45. A 149.

Melanotic

—6510.00. A 15.

Myxoma

—fetus. 6380.00. A 30.
—nose. 6380.10. A 15.

Papilloma

—venereal warts. 6450.00. A 15.

Sarcoma

—cystic of buttock. 6310.31. A 7.
—round-cell
—of forearm. 6310.18. A 7.
—and spindle-cell, of thigh. 6310.16. A 63.
—spindle-cell, of thigh. 6310.20.

Scirrhus

—of neck. 6470.00; 6470.05. A 15.

Serocystic

—6530.20. A 15.

Ulcer

—malignant, of hand. 8424 (M). A 107.

Unspecified tumors

—of buttock. 8786 (M).
—below the ear. 8781.1 (M).
—of face. 8788.5. (M).
—fatty, of arm. 6350.62.
—of groin. 8782 (M).
—of hand. 8753 (M); 8752 (M).
—from jaw. 6533.5.
—of neck. 8762 (M).
—from beneath quadriceps extensor. 6490.00. A 37.
—from scalp. 6534.26; 6534.27. A 15.
—of shoulder. 8781 (M)
—of thumb. 8755 (M).
—6500.00. A 37.

4. Gangrene

Gangrene

—foot. 6160.30. A 15.
—moist. 6160.20. A 15.
—dry. 6161.00. A 15.
—forearm and hand. 1313.00.
—hand
—moist. 6161.10. A 15.
—mummified, of child. 1319.20. A 15.
—phalanges, removed for gangrene following trench foot. 6161.10. A 55.

5. Wounds and Injuries

Bullet Wound

—6045.10; 6045.11.

Contracture

—of hand. 8416 (M); 8417 (M); 8418 (M).
—and cicatrix after burns
—of arm and forearm. 8411 (M); 8412 (M).
—of fingers. 8413 (M); 8414 (M); 8415 (M).

Skin wound of thigh causing gas gangrene. 6045.15. A 55.

(Conclusion of Part II; succeeding parts will appear in later issues.)

TRANSACTIONS & STUDIES

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President's Address*

By J. PARSONS SCHAEFFER

THE academic year 1948–49 of the College of Physicians of Philadelphia is about to come to a close. There remains the delivery of the annual address by the President at this Stated Business Meeting, this in accord with the Ordinances and By-Laws governing the administration of the College. It is of interest to recall that this College was instituted in January 1787 and incorporated in March 1789, bringing it to the advanced age of 162 years. Well may we feel honored in holding membership in this historic institution and through positive interest and faith acclaim its enviable record in the furtherance of scientific medicine and achieving worthy public relations.

As your retiring President, I shall review briefly the major activities of the College during the past year and bring you information bearing on the present status and the future needs of the College.

The total Fellowship of the College (as of December 27, 1948) numbers 829, of which 757 are Resident Fellows; 61, Non-Resident Fellows; 6, American Honorary Fellows; 3, Foreign Honorary Fellows; and 2, Honorary Associate Fellows. During the calendar year 1948, 41 new names were added to the roll of Resident Fellows; 3 Fellows and 1 Non-Resident Fellow resigned; and 1 Resident Fellow transferred to the status of a Non-Resident Fellow.

The Sections of the College have all been active during the year and at present are constituted as follows: Ophthalmology, 55 active members; Otolaryngology, 60 active members and 3 honorary members; General Medicine, 166 active members; Public Health, Preventive and Industrial Medicine, 38 active members; Medical History, 77 active members.

The College has suffered the loss by death of 12 Resident Fellows, 11 as of 1948 and 1, of 1947 previously unreported, and 2 Non-Resident Fellows, 1 as of 1948 and 1, of 1947 previously unreported. As individuals these Fellows were variously interested in the work of the College and participated in promoting its cause during the years of membership. In honor of the memory of the deceased, I would request the Fellows of the College in attendance here today to stand during the reading of the names of our departed friends and colleagues.

Resident Fellows

Solomon Solis-Cohen
Samuel McC. Hamill
J. Calvin Hartman
Charles F. Judson
H. Maxwell Langdon
Paul E. Loudenslager
J. Bernhard Menke
William Burrell Odenatt

* Delivered at the business meeting of the College of Physicians of Philadelphia, 5 January 1949.

Joseph Scattergood, Jr.
John Falconer Sinclair
T. Turner Thomas
Arthur W. Watson

Non-Resident Fellows

Guy Hinsdale
Charles H. Weber

It is of interest to record here that Dr. Solis-Cohen was a Fellow of the College continuously for a period of 60 years; Dr. Hinsdale, for 56 years; Dr. Hamill, for 54 years; Dr. Watson, for 53 years; Dr. Judson, for 48 years; Dr. Sinclair, for 45 years; Dr. Weber, for 44 years; Dr. Thomas, for 41 years; and Dr. Langdon, for 41 years. The other departed Fellows were connected with the College for much shorter periods. It is seldom that the Necrological List for a given year contains so many names with such lengthy tenures of Fellowship. What valued memory pictures these Fellows must have had of their long connection with the College, having in mind the many and important required changes in the activities of the College and the advances in the field of medicine.

On September 16, 1948, Dr. F. William Sunderman, the Secretary of the College, moved his residence to Cleveland, Ohio but continued as Secretary in a nominal manner up to the time of this Business Meeting of the College. The Council and Fellows of the College regret the loss of active participation by Dr. Sunderman. On certain occasions, however, he returned to the College and functioned at Council and Scientific Meetings. The Ordinances and By-Laws of the College made this arrangement valid. It became necessary, however, for some Fellow living closer to the College to take on the major and many auxiliary duties of Secretary until Dr. Sunderman's successor would be elected to the office. Fortunately, Dr. J. Harold Austin, a former Secretary, expressed his willingness to serve as Secretary, pro tempore whenever required. The College is indebted to Dr. Austin for his spirit and help at this time.

On the occasion of his removal from Philadelphia, Dr. Sunderman addressed a letter to the President of the College in which he says in part: "The welfare of the College has always been close to my heart, and it has been an especial honor for me to have been given the privilege of serving it. Please convey to the Fellows my fondest wishes for the continued success of our distinguished and venerable institution, of which we all are so justly proud."

On the basis of the anticipated revenue and expenditures of the College, the several appropriations recommended by the Finance Committee were voted by the Council in December 1947 and finally approved by the Fellows of the College at the Annual Business Meeting in January 1948. Because of unforeseen repairs and replacements the appropriation to the Hall Committee fell short of meeting the required expenditures of this Committee for the year. Fortunately there is now existent a moderate maintenance reserve fund for such contingencies and it is obvious that this fund must be drawn upon at times. It is equally patent that additions to this reserve fund of the College should and must be made from year to year in order that the College may advance its program unhampered and move forward with reasonable assurance.

Not only have the appropriations to the several College committees and certain officers provided for the many usual and required activities of the College but made possible repairs, replacements and installations as follows: A new vacuum system was installed, a much needed item; the water service from the street to the College Building was renewed; a new lantern equipment was supplied and new beaded screens were placed in Cadwalader and Mitchell Halls; the windows in Mitchell Hall were repaired; broken glass in the diffusing sash over the main stairway was replaced throughout. Many of the chairs in the Library were newly upholstered; a new roof was placed over the book-stack section of the College Building and the roof over the South Wing was repaired and the skylight well given attention.

Thanks are due the Hall Committee, Dr. William P. Belk, Chairman, one of the im-

portant Elective Standing Committees of the College, and the Superintendent of the Building for their constant interest and attention in caring for the physical plant of the College.

The eligibility of the various trust funds of the College for inclusion in one or other of two common trust funds—1) A Discretionary Common Trust Fund and 2) A Legal Common Trust Fund—as determined during the fiscal year 1947–48 and the execution of the plan during the fiscal year just closed has, it is believed, resulted in greater safety for these invested funds of the College. Certain funds of the College are restricted and cannot be pooled, that is, are not eligible for inclusion in either of the aforementioned common trust funds but each fund must be kept separate and apart from other funds as individual items in accord with specific requirements.

As anticipated, this change in the listing of the College's funds has enabled the Finance Committee of the College to consider more intelligently adjustments in the portfolio necessary in meeting the changing economic and financial conditions as they arose from time to time. Not only has resulted greater safety for the invested funds but the administration has been much simplified. The Treasurer has been benefited in preparing his annual report and the bookkeeping methods of the College have been placed on a more efficient basis.

Time and space will not permit to enter into details concerning the many and varied activities of the Finance Committee during the past year. It would, however, appear pertinent that mention should be made of one important transaction, this because of the general interest. It will be recalled that the lot at 13th and Locust Streets, owned by the College and the location of a former College Building, was for a number of years rented as a parking lot at a satisfactory income. During the past year the Finance Committee considered an offer to sell this property at what was believed a fair appraisal value by Mr. Meredith M. Jack. The conditions of the sale were presented to the Council of the College and on recommendation by the Finance Committee and approval of Mr. Eric A. McCouch, counsel of the College, the Council unanimously directed that the sale of the property be consummated for a total consideration of $100,000.00, $25,000.00 in cash and $75,000.00 to be represented by a purchase money mortgage, bond and warrant in form and substance satisfactory to the College and accompanied by title and fire insurance satisfactory to the College, payable within 20 years with interest at 4½% per annum, payable quarterly. The principal of the mortgage is to be amortized at the rate of 5% per annum for the first 5 years and at the rate of 3% per annum thereafter, payable quarterly. While it is believed that the income to the College for operating and maintenance expenses will be somewhat above that received when the property was rented, the cash payment and the amounts paid at intervals in the reducing of the principal sum of the mortgage will, of course, be invested and added to the capital funds of the College.

Throughout the year the Finance Committee, Dr. William D. Stroud, Chairman, and the Treasurer, Dr. David M. Davis, dealt with many problems having to do with changes in the financial structure of the College and in these troublesome times decisions frequently were made with difficulty and required much thought. Great appreciation is expressed to the Committee and the Treasurer for their constant attention and care. Miss Olga Lang also merits thanks for her faithful and efficient work as Clerk in the College Office. Main & Company, Certified Public Accountants, examined the accounts and records of the College for the fiscal year ended Nov. 10, 1948.

The Scientific Program of the College for the academic year 1948–49 began on February 4 with the delivery of the Thomas Dent Mütter Lecture LX by Balduin Lucké, M.D., on "Studies on Epidemic Hepatitis and its Sequelae." The next Scientific Meeting was a joint meeting with the Philadelphia County Medical Society on the evening of March 10. Thomas E. Jones, M.D., addressed a filled hall of interested and attentive listeners on the subject "Carcinoma of the Rectum." The Nathan Lewis

Hatfield Lecture XXXII was delivered on April 7 by Cecil James Watson, M.D., on "The Bile Pigments and Porphyrines in the Study of Jaundice and Liver Disease." This lecture was well attended. Murray J. Shear, PH.D., gave the Mary Scott Newbold Lecture LIX on the evening of May 5 on "Researches on Chemotherapy of Cancer." The scientific meeting on the evening of October 13 was held in Mitchell Hall and was again a joint session with the Philadelphia County Medical Society. Laurence H. Snyder, SC.D., addressed a goodly sized audience on "Genetics and the Practice of Medicine." The Alvarenga Prize Lecture VIII was delivered on the evening of November 3 by Melvin H. Knisely, PH.D., on "Sludged Blood." This lecture attracted the largest crowd of the year. Ernest L. Stebbins, M.D., gave the James M. Anders Lecture XXIII on December 1, speaking on the subject "Public Health and the Changing Order." The S. Weir Mitchell Oration XI was delivered by Thomas A. C. Rennie, M.D., on January 5, speaking on the subject "Psychiatry in Medicine and Society."

The Scientific Program for the year, arranged by the Committee on Scientific Business, Dr. George Morris Piersol, Chairman, brought to the College a distinguished group of scientists as speakers. Generally speaking, the lectures were well attended and I think it may be said that the Scientific Program part of the College's activity for the year was outstanding.

The meetings of the Sections of the College attracted goodly sized and interested groups and the officers of the Sections are to be commended for the success attained. The Section on Medical History in addition to its regular program arranged for nine lectures on "High Lights on Medical History" which were given on successive Friday evenings in Mitchell Hall of the College, beginning October 8, 1948. The students of the several medical schools and colleges of Philadelphia especially were invited to attend the series of lectures. At some of the lectures, Mitchell Hall was filled to capacity and at other times the attendance was much less. The prevailing opinion is that the series of lectures reactivated interest in the History of Medicine.

Pedro Francisco daCosta Alvarenga, of Lisbon, Portugal, an Associate Fellow of the College of Physicians, established a prize to be awarded annually by the College on each anniversary of the death of the testator, July 14, 1883. In consonance with this the College of Physicians as of July 14, 1948 awarded the Alvarenga Prize to Melvin H. Knisely, PH.D., formerly of the University of Chicago and now of the University of South Carolina, in recognition of his researches in the field of hematology. On the evening of November 3, Dr. Knisely delivered the Eighth Alvarenga Prize Lecture to a very large and attentive audience in Mitchell Hall of the College on the subject, "Sludged Blood."

As usual the Library Committee, Dr. Truman G. Schnabel, Chairman, has had a very busy year. In accord with the change in the By-Laws as voted by the Fellows of the College at the Business Meeting in January 1948, required contributions from Non-Fellows for the privilege of taking books out of the Library were permitted on and after July 1, 1948. The Librarian of the College reports that not only has this requirement been favorably received but from a financial point of view has proved helpful in augmenting the income derived from the major specific Library Funds and doubtless will continue to aid in advancing the cause of the College's greatest asset, namely, the Library. The Council of the College authorized the Library Committee to institute a schedule of contribution requirements per annum for certain categories of Non-Fellows who wish to take books out of the Library of the College. Such a schedule is now available and in use. It is not required here to elaborate more fully on this new contribution method. Mr. McDaniel, the librarian, to whom the Fellows and, indeed, all users of the Library are indebted for his deep interest and ability in directing the Library, has prepared a detailed report bearing on all phases of the conditions of the Library and its operation. This report

will be published in full in the *Transactions & Studies* and merits thoughtful reading.

The Mütter Museum continues to be a center of scientific interest. More than 1200 visitors, some of course casual observers but most of them seeking valued information, signed the Register. During the year Mrs. Wade, the Curator, working under the guidance of the Committee on The Mütter Museum, Dr. Oscar V. Batson, Chairman, completed the index of all the specimens and objects found in the Museum. The Committee's annual report will be published in full in the *Transactions & Studies* of the College. I would repeat what was said in the President's Address a year ago: "As Curator Mrs. Wade has shown herself courteous, attentive and capable." Much credit goes to her for the continued public interest in the Museum.

The Committee on Public Health, Preventive Medicine and Public Relations, Dr. Hubley R. Owen, Chairman, was again active in behalf of the College and continued to coordinate its efforts with other similar bodies in effecting better public relations and aiding and improving public health conditions in Philadelphia and its metropolitan area.

As usual the Committee on Entertainment, Dr. Gilson C. Engel, Chairman, merits praise for the attention it has given throughout the year in carrying forward the important work of the Committee. Visiting speakers appreciated the attention given them.

The College of Physicians had historic exhibits both at Convention Hall and in the College Building on the occasion of the Centennial Meeting of the Medical Society of the State of Pennsylvania in October 1948.

The *Transactions & Studies* of the College appeared quarterly under the direction of the Committee on Publication, Dr. Samuel B. Hadden, Chairman, and Mr. W. B. McDaniel, 2d, Editor. As usual the several numbers of the publication proved of much interest to the reader and of outstanding value to the College.

Council directed that the President of the College shall appoint a committee to survey and report on the present and probable early future needs of the College. This committee was appointed and is now functioning. Moreover, Council authorized the committee to solicit voluntary contributions toward a fund to defray the expenses of the survey, including the services of an architect and other needed expert opinion. The money for this survey has already been supplied voluntarily by a number of Fellows of the College. I am sure that all Fellows of the College will be much interested in the report of this important committee. Dr. T. Grier Miller is the Chairman.

In a recent letter, over the signature of the President of the College and directed to all Fellows, was briefly stated the necessity of increasing the income of the College for general maintenance and operation, repairs and replacements. A plan was offered for the consideration and vote of the Fellows at the January Business Meeting of the College—a plan which, if adopted, would not greatly burden the individual Fellow of the College financially yet would yield an over-all amount which, when added to other available income, would care for the more usual maintenance and operation costs and would provide for the repairs and replacements necessary from time to time in our forty-year old College Building and make it possible to add to the maintenance reserve fund for emergency purposes.

The plan mentioned in the foregoing paragraph has to do with the following: 1) The members of the Council of the College at their meeting on November 23, 1948, unanimously voted to recommend an amendment to the By-Laws raising the Annual Contribution to fifty dollars per year as of January 1, 1949 and 2) to recommend an amendment to the By-Laws making the initiation fee fifty dollars.

These amendments were regularly proposed at the Business Meeting of the College on December 1, 1948. This evening, January 5, 1949, on the occasion of the General Business Meeting of the College, the Fellows of the College unanimously voted approval of the changes in the By-Laws recommended by the Council of the College.

I now wish to express great appreciation to

the Fellows of the College for the action taken because it will greatly help in keeping our College building at the forefront of beautiful and well appointed formal Academic Medical Halls and will aid in adding to the administrative and service personnel of the College.

In conclusion, I am pleased to say that the College of Physicians of Philadelphia has had another very active and successful year, and as your retiring President I am grateful to the Officers, the Members of the Elective and Appointive Standing Committees, the Prize Committees and Trustees, and indeed all Fellows for their interest and participation in achieving this result. Then, too, I would be remiss did I not acknowledge the valued help of a number of employees of the College who, properly and willingly, integrated their several functions with the over-all work of the College. Without such coordinated effort the President of the College could accomplish little. I have enjoyed many years of active work in this College—my three years as President especially. I am grateful to the Fellows for the privilege of serving this historic College. And in vacating this Chair, I feel certain that the College of Physicians of Philadelphia will continue to move forward and upward in furthering the best interests of scientific medicine, in participating in the promotion of satisfactory health laws, and in varied ways concerning itself with the public welfare.

I now yield to my friend and successor, Dr. T. Grier Miller, who has given much time over a period of years in the interests of this College and I feel certain that one of his chief interests if, indeed, not his first interest, apart from his family, will continue to be the College of Physicians of Philadelphia. Dr. Miller, I bespeak for you every success and happiness as President and would ask that you accept this gavel and occupy the Chair I am leaving.

Memoir of Samuel McC. Hamill*

By WILLIAM R. NICHOLSON

DR. Samuel McClintock Hamill, son of the Reverend Robert Hamill, D.D. and Margaret E. Lyon, was born at Oak Hall, Center County, Pennsylvania, on November 3, 1864 and died in Philadelphia May 3, 1948. He was named for his uncle, also a Presbyterian clergyman. His father had been Moderator of the Synod of Philadelphia, and later also of the Synod of Harrisburg, and the family had been associated with the Presbyterian Church in Scotland, even before Dr. Hamill's forebears came to this country early in the eighteenth century. Dr. Hamill had three brothers, now deceased, and two sisters who survive him. He attended the Lawrenceville School and Princeton College, and entered the Medical School of the University of Pennsylvania in the Class of '88, being President of that Class at the time of his graduation. After his graduation he became Resident Physician at the Philadelphia General Hospital and started his practice immediately after finishing his term there.

In 1895 he married Lila Clarke Kennedy of Philadelphia, who died last year. By this marriage he had three sons, all of whom survive him. For several years in his young professional life he served as Demonstrator in the Medical Department of the University of Pennsylvania, doing his work in the hospital of that institution, but his interest was always primarily in the Department of Children's Diseases, and in 1901 he became Professor of Diseases of Children in the old Polyclinic Hospital, of blessed memory. He was much interested in the then new Social Service activities and was one of the founders of that department at the Polyclinic Hospital. He was also an early enthusiast in the work of the Community Chest in Philadelphia, always giving it most liberal support. At the time of the amalgamation by the University of Pennsylvania of the Polyclinic Hospital and the Medico-Chirurgical College Medical School, to form the Graduate School of Medicine of the University of Pennsylvania, Dr. Hamill was elected Professor of Diseases of Children in that institution. He was a staff member at various times in his early life of St. Christopher's Hospital, the Howard Hospital and the Presbyterian Hospital, in each institution being associated with the Department of Diseases of Children. In the very early days of the century he was Pediatrist at the Maternity Hospital. Dr. Hamill was one of the founders of the Philadelphia Pediatric Society and was its President in 1901. In 1911 he became Chairman of the Section on Diseases of Children of the American Medical Association. In 1913 he was elected President of the American Pediatric Society and in 1915 he was President of the American Association for the Study of the Prevention of Infant Mortality. In 1917 he became a member of the General Medical Board of the Council of National Defense, and in the same year he was a Director of Child Welfare for Pennsylvania and Chief of the Division of Child Hygiene of the Pennsylvania State Department of Health.

In 1932 he became President of the American Academy of Pediatrics, of which he was one of the founders, and in the same year he also became President of the American Child Welfare Association. He had been a member of the Board of Managers of the Babies' Hospital and at one time he was a member of the Board of Trustees of the Lawrenceville School, and President of the Society of the Alumni of the Medical Department of the University of Pennsylvania. During President Hoover's term he was appointed Chairman of the White House Conference on Child Health.

* Read at the meeting of the College of Physicians of Philadelphia, 1 December 1948.

To return again for a moment to his early life, he became a Fellow of the College of Physicians of Philadelphia in 1894 and but a few years later he was made the Chairman of the Committee for raising funds for the present building and he did yeoman service. When one realizes that at the time of his appointment as Chairman of this Committee he had been a Fellow of the College for only a few years, and if in addition it is realized that the men then prominent in the College of Physicians of Philadelphia were, among others, George de Schweinitz, Horatio C. Wood, William J. Taylor, S. Weir Mitchell, Richard S. Hart, John Ashhurst, Jr., W. W. Keen, Thomas R. Neilson et al., it speaks for a definite recognition of his ability by men who only gave honor where honor was due.

In 1940 the University of Pennsylvania gave him the Honorary Degree of Doctor of Science, in recognition of his work in child health. He had also been recipient of the Strittmatter Medal of the Philadelphia County Medical Society.

The foregoing is the history of a full and well spent professional life, and such a record deserves a most honorable place in the memorabilia of the College of Physicians of Philadelphia. But something more must be said about him, for the information of the many younger Fellows of the College who did not know Dr. Hamill, a fact which is easily understood when it is remembered that at the time of his death he was the third oldest living Fellow of the College, and also that for the past several years his activities had been much curtailed by ill health. I had the honor of his close friendship for the past fifty years, an honor indeed, and therefore I can speak of his personality with intimate knowledge. While he had been an invalid for many months, as has been said, and while his bodily activities had been curtailed, his interest in his life work, the care of children, remained unabated, and his aptitude for friendship also was unchanged. His keen sense of humor continued to be a delight, while his ideals remained as they had always been, of the highest, and his sympathies were just as far-reaching as ever.

Would that words of mine might portray him to you as he was, and as I knew him! A loyal friend and a gentleman of the old school.

Annual Report on the Library*

The Year in Review

The statistics that follow argue eloquently enough for the general health of the library. Attendance, circulation, acquisitions, subsidiary services (inter-library loan and photostat) show marked and gratifying advances, except for the photostat service, which was inoperative now and then for varying unavoidable reasons. Most significant was the rise in attendance, in the number of volumes consulted in the library, and in use of the inter-library loan service. The former two are of course the truest indexes to a library's value to the immediate community. At the same time, the use of its inter-library loan and photostat services provides a valuable, if incomplete, index to what the library has been able to contribute to other libraries, and thus to individuals, at longer range.

Our efforts to meet these increased demands were very greatly aided, let it be said forthwith, by the continued annual grant of $1,000 from the Smith, Kline & French Laboratories; and by added income derived from a new policy on borrowing privileges, described immediately below.

The New Policy on Borrowing

In July, the library, with the approval of the Fellows, took a step forward that was unprecedented in its history. Previously, borrowing privileges were extended gratis to any one nominated for them by a Fellow, and inter-library loans were extended freely to commercial and non-profit organizations alike. The result, in the years since the privileges began to be accorded more freely than they had been, was that the library finances and staff were increasingly hard put to it to meet the demands, while the Fellows not infrequently found themselves on the outside looking in on a library which their annual contributions were helping to support.

The solution adopted was one already successfully in use by comparable institutions. The principle governing it is that, while the library must continue to be absolutely free to the extent that any one is entitled to use its facilities on the premises, the borrowing privilege is a special one for which it is only fair to require a supporting contribution. Nevertheless, it was decided to interpret the principle as liberally as possible in practice. As finally adopted, the plan permits the Fellows to confer free borrowing privileges on their personal assistants; on undergraduate medical students and hospital internes; and on short-time visitors in the city. It is expected that other individuals wishing the privilege will fall under one or another of six categories; and a contribution requirement was set for each category, first, on the basis of whether or not the individual was eligible for fellowship; and second, on the basis of what seemed like a reasonable contribution to be expected from persons in the given category, as balanced against the library's non-profit services. A separate category was set up for commercial organizations. Inter-library loans to non-profit institutions are unaffected by the plan.

In general, the new policy has been well received and promises to achieve its purposes. Though its details were long and carefully worked out in advance, they are not regarded as immutable. Modifications may very well be made in the light of experience of the plan in operation. Any factor tending to limit use of the library is to be deplored. It may well be that the attendance and circulation figures next year will indicate that hundreds of those who held free borrowing privileges have not found it possible or desirable either to make the contribution or to do their reading in the library. That would be extremely unfortunate. On the other hand, this would have to be balanced by the knowledge that the library was able to give better service to those

* 1 November 1947–31 October 1948.

with the greatest claim on it, even as it continued to do all in its power for all. We shall hope, however, that in time the library will exert a pull sufficient to draw into its orbit, for reading or borrowing, every last wight capable of drawing something good from it.

Historical Collections

The statistical part of our report shows the general features of the library's operations, but it does not, of course, begin to indicate what goes on behind the surface plane, which is, naturally, in two dimensions only. One may justifiably assume, from the statistics, that the library kept its nose close enough to the ground, when it came to providing in one way or another the daily bread; but a library with the rich historical resources that this one owns must do more than fill its windows with fresh loaves every day, if it is to live up to its kitchen. Unfortunately, circumstances have denied any planned development of these important resources, which have, nevertheless, been added to or aided in ways which it seems appropriate to record in an annual report.

As last year, it will not be possible to list by name all of the historical acquisitions; and, again, selections have been made to indicate types of material welcomed by the library, since experience shows that the inexperienced donor often hesitates to offer material in the modest belief that, since it is likely to have little market value, it would not be welcomed by a large library.

Our former chairman, later president of the College, Dr. Krumbhaar negotiated the library's receipt of a number of interesting historical possessions of the late Dean William Pepper; notably, 5 Osler letters, none of them appearing in Cushing's biography of Osler; a photograph of the Servetus statue at Annemasse, with a note by Osler on the back; a photograph album containing photographs of prominent European physicians of the mid-19th century; a Benjamin Rush publication inscribed with the signature of John Archer, the first graduate of the first medical school in the American Colonies. Aside from these, and many donations of current books and journals, Dr. Krumbhaar also enriched the library by the gift of files of personal letters from many of the most noted medical men of the day, and by nearly complete series of programs of the University of Pennsylvania's Undergraduate Medical Association, and the Cosmopolitan Medical Club. No one who has not looked, often in vain, for primary source material of this sort can quite comprehend, possibly, the gratitude that is extended the library that can produce it. Another Fellow, Dr. William S. Wadsworth, has similarly made lighter the researches of future historians by presenting scrapbooks containing series of programs of other local medical societies, as well as albums of pictorial material that add appreciably to what the library previously had.

Source material of another sort is a card-file of graduates of the old Medico-Chirurgical College, and other bodies, kept by our late Fellow Dr. A. C. Morgan and presented by our Fellow Dr. Robert J. Hunter. This file had been installed but a short while when it first provided requested information of a personal sort that the library could certainly not otherwise have furnished and that it is doubtful any other existing information service could have produced.

Still another interesting, and sometimes decisive, source of historical information is the medical school diploma and the medical society certificate of membership. Our collection of these was importantly increased by our nonresident Fellow and ever thoughtful friend, Dr. W. A. N. Dorland, of Chicago, who presented a very fine group of medical diplomas and certificates awarded his father around the middle of the last century, as well as some of his own. The designs and signatures involved, aside from their pragmatic value, have a very great appeal to the imagination of those interested in the history of American medicine.

A sister library, the Boston Medical Library, presented what was to it a duplicate copy of a collection of ancient medical texts published by the Aldine press, in 1547,under the title *Medici Antiqui*. Our surprise that the library did not

already have this collection of classic texts from so famous a press was exceeded only by our gratitude to Mr. Ballard, the director of the library, for offering it to us. This copy, as an inscription shows, was in early days the property of Petrus Pipernus, an Italian physician and philosopher of the mid-17th century, several of whose writings are in the library.

Through Dr. Bradley, Dr. H. H. Perlman presented a copy of Ernst Gottfried Baldinger's *Historia mercurii et mercurialium medica*, 1783. This army surgeon, Baldinger, was a prototype of the several well-known Army Medical Corps historians of our day, and contributed a number of valued historical and biographical studies, not by any means confined to military medicine. His bi-partite medical history of mercury and the mercurials is obviously a welcome addition to the other publications of his that we already had.

The field of popular medicine is represented by a broadside advertisement, in German, of liverwort syrup, published by a prominent Philadelphia dispenser of nostrums in the first half of the last century, G. W. Carpenter, whose medicinal products, on the evidence of the broadside, were not unknown to the Pennsylvania Dutch of Lancaster County. This was the gift of Dr. J. J. B. Light.

The medical stamp collection was further added to by our Fellow Dr. G. N. J. Sommer.

The year saw also the realization of the "Paul Judd Sartain Library of Ophthalmological Illustration," in accordance with the bequest of Dr. Sartain, a Fellow, who died in April, 1944. The Section on Ophthalmology was invited by the Library Committee to designate one of its members as advisor on the development of the collection. Dr. Burton Chance, long-time member and former chairman of the committee, was so designated by the Section, and it is hoped that, with his expert guidance, the collection may become of considerable use to our ophthalmologists.

It is a matter of regret that circumstances made it impossible to prepare as many exhibits as we would have liked. If these are to be both instructive and stimulating, considerable time and thought must go into the selection and arrangement, especially when the resources available are so extensive as those our library provides. Perhaps the most satisfying of those offered during the year was one prepared in commemoration of the centennial of the State Medical Society. Devoted to medical journals published in 1848, it showed that the physician of that day could not plead innocence of medical advances for lack of their prompt publication, and, at the same time, showed the same duplication of effort by review and abstract journals that is of concern to us today, when the numerous indexes and large libraries now available give even less reason for such wasteful duplication. Smaller, period exhibits were provided for the series of weekly lectures on medical history presented by the College's Section on Medical History.

Dr. George B. Wood has been going over the large amount of uncatalogued manuscript material in the library's George B. Wood (1797–1879) collection, sorting the material into categories and in other respects reducing it to manageable form. It need hardly be said how grateful the library is for this exceedingly appropriate assistance. Dr. Wood's study has already turned up interesting non-medical material that the Historical Society of Pennsylvania and the American Philosophical Society were happy to receive, on offer of our Library Committee. Dr. Wood also prevailed upon his friend Prof. J. Percy Moore to survey the Joseph Leidy manuscript material received a few years ago, with the result that rather more specific knowledge of what is available therein can be furnished a future biographer of Dr. Leidy.

Annual Meetings

The library was co-host or adjuvant to two national associations holding their annual meetings in the city, one following close on the heels of the other. Arrangements for the 50th anniversary meeting of the Medical Library Association, founded in this city and with our then-librarian, Mr. Charles Perry Fisher, as a charter member, occupied no inconsiderable

share of the attention of the staff for some months in advance—notably that of the assistant librarian, Miss Manson, who was chairman of the committee on arrangements, and, by common consent, a superb one. The meeting of the American Association of the History of Medicine, with its sessions held in the College building, drew only in minor fashion on the staff's assistance, of course.

Activities of the Staff

An incalculable blow was sustained late in the library year, when Miss Manson, our greatly admired head cataloguer and assistant librarian, left us to head the Lane Medical Library of Stanford University, commonly regarded as the preeminent medical library of the far west, which borders on her native heath. Her patience and tact and selfless devotion to duty during her six years of service to the library were of a sort rarely encountered and inevitably left an uncomfortable void on the personal plane; even as we cannot, who know of her successful efforts to make more of the libary's hidden resources useful, view too lightly the loss of those services. But there is also a deep sense of satisfaction that such fine recognition has come to one who so richly deserved it. Miss Eunice E. Sharp was engaged to succeed Miss Manson.

Following the meeting of the Medical Library Association, our assistant in charge of the current-periodicals room, Mrs. Elizabeth F. Bready, was appointed chairman of the Association's Committee on Medical Periodicals and Serials. Mrs. Maud G. Maines, assistant in charge of the reading room, was elected treasurer of the Social Sciences Group of the Special Libraries Council of Philadelphia. While such activities may seem to deflect attention from the assistants' daily duties, actually the wider acquaintanceships and general knowledge gained result in far more proficient and understanding handling of the routine work. And it may be argued peaceably that one of the functions of a large research library is to encourage its personnel to provide the sort of professional leadership that is essential if libraries are to function at all coherently in an incoherent world.

Aside from his usual College engagements, the librarian continued to hold a seat on the Medical Library Association's Committee on a Comprehensive, Coördinated Abstract Journal for Clinical Medicine. A brief communication on editing, from his pen, was printed in *Science* 106: 491, 21 Nov. 1947.

The roster of the library staff, as currently constituted, follows:

Librarian
W. B. McDaniel, 2d

Assistant Librarian and Head Cataloguer
Miss Eunice E. Sharp

Assistant in Charge of the Reading Room
Mrs. Maud G. Maines

Assistant in Charge of the Periodicals Room
Mrs. Elizabeth F. Bready

Assistant Cataloguer
Miss Gertrude C. Cirotti

Secretary to the Librarian, and General Assistant
Miss Kathryn E. Haegele

Photostat Operator and Page
Miss Vilma Harmon

Pages
Miss Kathryn Houston
Miss Ida Hund

Inventory

	1948	1947
Total number of accessioned[1] items	168,925	167,200

	1948	1947
Incunabula	415	415
Manuscripts (including a few typescripts)	695	677
General	167,815	166,108
	168,925	167,200

	1947	1948
Total number of unaccessioned[1] *items*	322,593	321,240
Reports	26,749	26,655
Periodicals "reserve"[2]	7,267	6,084
Theses and Dissertations	52,961	52,299
Pamphlets	235,616	236,202
	322,593	321,240
Total number of current periodical publications regularly received	1,297	1,169
Portraits[3]	70,735	66,081

Distribution of This Material

	Accessioned Items	Unaccessioned Items
General Library (including the Lewis Library)	164,690	322,589
On permanent deposit:		
Gross Library	3,818	4
Parry Library of the Obstetrical Society of Philadelphia	217	0
Mütter Museum[4]	200	0
	168,925	322,593

Current Periodicals

	Purchase	Exchange or Gratis	Annuals	Total
U. S. A.	260	303	42	605
Western European Continent	355	10	6	371
Latin America	29	75	4	108
United Kingdom and Eire	101	31	4	136
Canada	3	19	2	24
Eastern European Continent	5		1	6
Asia	15	10		25
Africa	5	5	1	11
Pacific Area	2	9		11
Grand Totals, 1948	775	462	60	1,297
Grand Totals, 1947	625	508	36	1,169
Grand Totals, 1939	688	514		1,202

New titles: A total of 89 periodicals was added to the Norris Room in 1947–48. Sixty-seven of these were purchased, 22 received in exchange or gratis. There were 70 that began with volume 1.

Separate Issues received, checked-in on the cards, and shelved totaled 11,952. In addition, thousands of duplicate issues were received, as usual; 1,103 of these were retained for our 'reserve' files, no attempt being made to count those held merely for exchange or other use.

Visitors to the Norris Room for the year totaled 5,883.

[1] Our 'accessioned item', or 'volume', normally contains not fewer than 100 pages, usually is bound, and always is catalogued. It may comprise a part of a 'book' or periodical 'volume', one or more complete 'books' or periodical 'volumes', a collection of reports, pamphlets, or theses. In a few instances, the term applies to miscellaneous items such as a photograph album or a large collection of correspondence or private papers.

The 'unaccessioned item' is intended to apply to (usually unbound) pamphlets, reports, theses, or other material of fewer than 100 pages; only a part of this material is catalogued. It should be stressed, however, that in this category are included uncounted thousands of reports and theses of 100 pages or over, as well as smaller classic items, which would quite properly figure in the 'number of volumes' claimed by other libraries, and which would indeed figure among our 'accessioned items', had our predecessors and we ever been able to accession and catalogue them.

[2] More-or-less complete duplicate volumes of important and much-used periodicals.

[3] Including 118 oil, and 429 other, framed portraits in the care of the Committee on College Collections. The count of portraits represents the number of entries on the cards in the portrait catalogue. The entries represent, in turn, both loose portraits and those in books, many of them, of course, being merely different reproductions of a single original.

[4] The books of the Mütter Museum are not permitted to be removed from the College building.

Readers' Use of the Library

Library Hours. The library was open, during the academic year, from 9:30 to 9:30 on Mondays and Wednesdays; from 9:30 to 5:30 on the other weekdays. During June, July, August, and the first half of September the library was open from 1 to 9:30 on Wednesdays; from 9 to 5 on the other weekdays, except Saturdays, when it was closed. The following legal holidays were observed: Thanksgiving (beginning at 5:30 the preceding evening), Christmas and New Year's (beginning at 1 on the preceding days), Memorial, Independence, and Labor Days. The library was also closed 29 May, because of the Medical Library Association's meeting.

Number of visitors:

	1948	1947	Totals 1948	Totals 1947	Totals 1939
Days (including evenings)	(293)	(289)	15,777	14,501	12,746
Circulation of books:					
Number of volumes taken out (Books: 2,892; Periodicals: 4,528)			7,420	8,107	8,524
Number of volumes consulted in the library[5]			71,720	56,245	49,725

Inter-library loans: The library sent 2,164 (1947: 1,813) volumes on inter-library loan to 140 (1947: 94) libraries in 25 (1947: 27) States and has borrowed 7 (1947: 2) volumes from 4 (1947: 1) libraries.

Photostats: 3,120 photostatic prints were furnished on request (1947: 3,752).

Acquisitions and Accessions

Accessioned Acquisitions:

1948: 1,725 volumes (1,056 by purchase; 507 by gift; 162 by exchange). (Books: 778; Periodicals: 947).

1947: 2,198 volumes (1,336 by purchase; 716 by gift; 146 by exchange). (Books: 923; Periodicals: 1,215).

Non-accessioned Acquisitions:[6]

1948: 384 Pamphlets (1947: 336).
94 Reports (1947: 701).
662 Theses (1947: 800).

Donations

The individual donors for the past year number 281 (1947: 317). The library is indebted for large gifts of books, pamphlets, and unbound periodicals to the following donors:

Dr. S. Bellet; Blakiston Co.; Boston Medical Library; Drs. K. Chouké, J. V. Klauder, E. B. Krumbhaar; Lea & Febiger; Dr. W. E. Lee; J. B. Lippincott Co.; Philadelphia Bibliographical Center; Philadelphia County Medical Society; Rockefeller Foundation; W. B. Saunders Co.; Smith, Kline & French Laboratories; South African Institute for Medical Research; University of Pennsylvania; Drs. W. S. Wadsworth, I. Wolman; Woman's Medical College; Wyeth, Inc.

Various publishing houses have presented volumes as follows: Blakiston Co., 26; F. A. Davis Co., 13; Lea & Febiger, 12; J. B. Lippincott Co., 24; W. B. Saunders Co., 45.

Other individual donors were as follows: Drs. E. Aegerter, J. W. Allen, M. Asbell; Mr. B. M. Baruch; Mr. H. R. Bickerton; Drs. W. G. Bowerman, C. Bridenbaugh, E. T. Bunje, C. C. Burlingame; Mr. L. H. Butterfield; Drs. W. W. Cadbury, A. M. Chesney, B. Chance, M. Solis-Cohen; Prof. I. DeB. Daly; Drs. N. S. Davis, 3rd, W. A. M. Dorland; Prof. E. Earnest; Drs. L. Edelstein, A. A. Eshner, L. K. Ferguson, J. A. Flaherty; Mr. J. E. Gibson; Dr. J. G. Gibson; Mr. R. W. Greene; Drs. F. M. Groedel, S. McC. Hamill (Estate), J. W. E. Harrisson, W. Haymaker, A. E. Hoag, H. E. J. Houssay, M. Jessner; Rev. N. S. Johnston; Drs. C. F. Judson, H. T. Kelly; Mr. E. F. Knipling; Drs. A. Koerner, C. D. Leake, S. S. Leopold, R. L. Levy, J. J. B. Light; Miss C. Manson; Drs. J. W. McConnell, T. H. McGavack; Mrs. H. L. Merscher (Estate of Dr. H. L. Merscher); Drs. M. T. Moore, A. C. Morgan (Estate through Dr. R. J. Hunter), H. E. Morton, W. R. Nicholson; Miss J. Oppenheimer; Dr. F. R. Packard; Miss E. Patton; Drs. W. Pepper (Estate), D. B. Pfeiffer, E. F. Roberts, K. F. Russell, T. Scattergood (Estate), J. P. Schaeffer, L. C. Scheffey, T. G. Schnabel, W. F. Sheldon, E. Shorr, H. C. R. Simons, G. N. J. Sommers,

[5] The number of volumes "consulted in the library" includes only those supplied on demand. Readers have access to the bound volumes of periodicals and reference works kept on the shelves in the Reading Room; the Fellows, and occasionally others, by special permission, have access to the book-stacks. There are, therefore, many volumes consulted of which no accurate record can be kept.

[6] As usual, not all the pamphlets, theses, and numbers of various journals listed as received had been checked for keeping or discard at the close of the library year.

S. G. Stewart; Mr. J. R. Stubs; Drs. A. W. Tallant, E. W. Thomas, J. M. Thorington, H. R. Viets, H. Wastl, J. H. Welsh, A. S. Wiener; Dr. & Mrs. J. W. Wister; Drs. A. C. Wood, G. B. Wood, W. Zentmayer.

Exchanges

The *Transactions & Studies* was sent, either as gift or in exchange, to 305 organizations.

The library received a number of journal issues through the Medical Library Association Exchange.

Theses and dissertations to the number of 662 have been received on exchange from the following European schools of medicine: Universities of Amsterdam, Basel, Bern, Copenhagen, Geneva, Köln, Lausanne, Leiden, Louvain, Tübingen, Utrecht.

Work of the Cataloguers

	1948	1947
Accessioned items catalogued or recatalogued	744	842
Unaccessioned pamphlets and Fellow' reprints catalogued by author or by author and subject	1,791	1,359

W. B. McDaniel, 2d
Librarian

Approved:
Truman G. Schnabel
Chairman

LIBRARY OF THE
COLLEGE OF PHYSICIANS
OF PHILADELPHIA

Annual Reports of the Committees on the Mütter Museum and College Collections

The Museum

The museum was open to Fellows of the College, physicians and the general public on all days when the College building was open, from 10:00 to 1:00 and from 2:00 to 5:00 except Saturdays, when the hours were from 9:30 to 1:00. The museum was also open on the evenings of the Stated Meetings of the College. The curator reports that there were 1242 visitors to the museum during the year, many of whom were students from the Dolan College of Embalming, the Pennsylvania State College of Optometry and the Franklin School of Medical Technology.

The Sixtieth Thomas Dent Mütter Lecture was given February 4, 1948, by Balduin Lucké, M.D., who spoke on *Studies on Epidemic Hepatitis and Its Sequelae*. The lecture was published in the April 1948 issue of *Transactions & Studies* of the College.

Part II of the Catalogue of the Mütter Museum appeared in the December 1947 issue of *Transactions & Studies* of the College. The entire catalogue, with the exception of the index, has been completed by the curator and committee, and will be published in subsequent issues.

Dr. Theodore F. Bach used many of the arthritic specimens to illustrate a lecture held at the College.

Mrs. Ella N. Wade was reappointed curator and clerk-technician for the year 1947–1948.

Accessions to the permanent collection of the Mütter Museum for the year, and falling under the provision of the Mütter Deed of Gift, are as follows:

Presented by William S. Wadsworth:

- Craniometer devised by Dr. Wadsworth
- Gigli's wire saw
- Dr. Battershall's inhaler
- Hutchinson's stomach pump
- Brass lever stomach pump
- Dennison's stethoscope
- Hawksley's stethoscope
- Double screw hook for nasal polypus
- Goodwillie's nasal speculum
- Septum splint
- Skene-Folsom's urethral speculum
- Three hard rubber rectal specula
- Two pleximeters
- Liston's spring-action artery forceps
- Two slide-catch artery forceps
- Instrument for grasping tumors
- Meatotome
- Three Peaslee's tubes for intra-uterine medication
- Two sponge holders
- Thomas-Cutter stem pessary
- Two Murphy buttons
- Rectal irrigator
- Dean's ear snare
- Robert's tonsil seizing and haemostatic forceps
- Urethrotome
- Lithotomy forceps
- Tenaculum forceps
- Ligature carrier
- Chest piece for stethoscope
- Two tampon expellors
- Four Bush's needle holders
- Cutting and holding scissors
- Two double edged knives
- Two pair of double action scissors
- Mouse tooth forceps
- Two aspirator needles
- Three ear forceps
- Enucleation forceps
- Section knife with two blades
- Allingham's ligature carrier
- Instrument for enlarging corneal incision
- Two Brunetti's chisels
- Set of postmortem instruments formerly belonging to Dr. Judson Daland
- Postmortem knife

Complete set of dental tools about 100 years old
Vaginal speculum
Periosteum elevator
Periosteum raspatory
Tonsil seizing forceps
Bistoury
Spoon and curette
Three applicators
Knot-tier
Agnew's instrument for adjusting sutures
Bush's forceps for withdrawing needles in operation upon piles
Caustic carrier
Postnasal applicator
Tenaculum for vesico-vaginal fistula

The College Collections

Mrs. Ella N. Wade was reappointed custodian of College Collections.

Accessions to the College Collections were as follows:

Presented by Miss Josephine R. Howell:
Oil portrait of her grandfather, Dr. Joseph G. Richardson.

Presented by Henry R. and Marguerite L. Glentworth:
Oil portrait of their great-grandfather, Dr. Plunket F. Glentworth, by Gilbert Stuart.

Presented by Marguerite L. Glentworth:
Oil portrait of her great-great-grandfather, Dr. George Glentworth, by Rosenthal.

Presented by Dr. George B. Wood:
Oil portrait of his great-uncle, Dr. George B. Wood.

Presented by Dr. Francis R. Packard:
Medicine bag formerly belonging to Dr. George Randolph Parry.

Presented by Dr. J. Monroe Thorington:
Medal presented to Dr. Thorington by the Mead Johnson & Company as a token of appreciation for his participation in the Ninth Annual Exhibition of the American Physician's Art Association, Atlantic City, 1947.
Medal of Award to Dr. J. Monroe Thorington from the American Physicians Art Association, 1948.
Seven wax votive offerings, modern, but cast in ancient moulds.
Iron votive animal of St. Leonard, early 17th century. Bavarian, or Tyrolese.
Two silver votive offerings.
Small figure of the Black Madonna from Switzerland.
Small silver medal of the Black Madonna.
Votive painting of the early 18th century. Bavarian.
Three medals:
Dr. Johann Heinrich Lochner
Dr. Albert Haller
Dr. Louis André Gosse

Presented by Dr. Burton Chance from the collection of Dr. Paul Sartain:
Dissecting instruments
Pocket case of instruments

Presented by Dr. I. T. Wolman:
Badge of First International Poliomyelitis Conference, New York, 1948.

Presented by Dr. Edward F. Corson:
Two medals—
South Africa—Rhodesia 1896
British medal of the Challenger Expedition, 1886–1895

Presented by Dr. D. Sergeant Pepper from the effects of Dr. William Pepper:
Bas-relief of Fothergill
Miniature of Dr. Thomas Bond
Liquid medicine in a leather case
Persifor Fraser's Apothecaries' set of powdered and liquid medicines
Doctor's bag
Spring lancet
Cupping set
Four obstetrical instruments used by Dr. Christopher Heydrick who graduated from the University of Pennsylvania in 1792:
Vectis
Solid blade vectis
Crotchet
Obstetrical Forceps
Box of animal thermometers and photostat of record in Pasteur's hand-writing.
Gavel presented to Dr. William Pepper when he was President of First Pan-American Congress, Washington, D. C., 1893.

Collection of the following medical medals:
- Dr. Ulysse Aldrovandi
- Asclepios der Heilende
- American Medical Association
- Sir Robert Barker
- Baron Dr. Jons Jakob von Berzelius (2)
- Dr. Marie Francois Xavier Bichat (3)
- Dr. Theodor Billroth
- Dr. Johann Friedrich Blumenbach (2)
- Dr. Herman Boerhaave
- Dr. Sir Benjamin Collins Brodie
- Dr. Victor von Bruns
- Dr. Maurizio Bufalini
- Count Dr. Georges Louis Le Clerq de Buffon (2)
- Dr. Girolamo Cardano
- Dr. Giuseppe Cervi
- Delft Charity Medal
- Dr. Vincenzo Chio
- Civic Hospital, Trieste, Italy
- Dr. Carlo Colleix
- Dr. James W. Cusack
- Baron Georges Leopold Chretien Frederic Dagobert de Cuvier (2)
- Famine medal—Thuringia 1771
- Famine medal—Germany 1816–1817
- Dr. Jean Fernel
- Dr. Girolamo Frascatori
- Dr. John Freind
- Dr. Franz Joseph Gall (3)
- Dr. William Wood Gerhard
- Dr. Daniel Eberhard Guenther
- Dr. Joseph Ignace Guillotin
- Dr. Daniel Henrik Guyoy
- Dr. Albrecht von Haller
- Rene Just Hauy
- Friederich Heinrich Alexander von Humboldt (3)
- International Hygiene Exhibition, London 1893
- Baron Joseph Franz von Jacquin
- Dr. Adrien L. de Jussieu
- Kissingen Medical Springs
- Dr. Robert Koch (4)
- Krankenhaus, Hamburg, Germany
- Dr. Justus von Liebig
- Lunatic Hospital, Hamburg
- Manchester Infirmary, England
- Faculty of Medicine, Paris (2)
- Lead medal with "Mercurus" (unidentified)
- Methodist Episcopal Hospital, Philadelphia
- Dr. Giovanni Battista Morgagni (2)
- German Naturalists and Physicians XXXII Congress, Vienna 1856
- Sir Isaac Newton
- Dr. Lorenz Oken
- Dr. Heinrich Wilhelm Olbers
- Dr. Matthieu Joseph Bonaventure Orfila
- College of Pharmacy, Paris
- Dr. Edmund Alexander Parkes
- Dr. Christoph Heinrich Pfaff
- Dr. Guy Poter
- Red Cross—Brussels
- Red Cross—Holland
- Dr. Francesco Redi
- Dr. Johann Ludwig Regemann
- Dr. Giovanni Rasori
- Henry D. Rinsland medal (unidentified)
- Baron Karl von Rokitansky
- Roman medal (unidentified)
- Royal Hospital School, Greenwich, England
- Royal Infirmary Medical School, Liverpool, England
- Dr. Carl Asmund Rudolph
- Dr. Benjamin Rush (3)
- Dr. Luigi Sacco
- Carl Wilhelm Scheele
- Baron Dr. Louis Joseph Seutin
- Italian Scientist III Congress, Florence, Italy
- Dr. Philipp Franz von Siebold
- Smallpox, Paris
- Societe de Medecine, Paris
- Societe de Medecine Legale, Paris
- Dr. Johann Stielgitz
- Dr. William Stukeley
- Academy and School of Surgery, Paris
- VI International Congress of Surgery, London 1923
- Dr. Robert Lawson Tait
- Dr. Frederick Tiedmann
- Dr. André Vesalius
- Vienna Veterinary College

Vienna Military Medical College
Count Alessandro Volta
Dr. Francis Willis (2)

Presented by Dr. Edward B. Krumbhaar:
Haemoglobinometer
Dare's haemoglobinometer
Small ivory microscope with three ivory slides
Warm stage
Early mechanical stage
Two apothecaries' scales
Pair of old spectacles
Knives for frozen sections
Camera lucida
Early duodenal bucket
Record hypodermic syringe
Hemocytometer
Hooker's venous pressure manometer
Collection of medical medals:
Academy of Medicine, Paris
Dr. Georgio Baglivi
Dr. Hyacinth Theodor Baron Sr.
Dr. Marie Francois Xavier Bichat (2)
Dr. Theodor Billroth
Civic Hospital, Trieste, Italy
Baron Ernst von Feuchtersleben
Dr. Johann Peter Frank
Galileo Galilei
Dr. Franz Joseph Gall
German Hospital, New York
Dr. Joseph Ignace Guillotin
Dr. Samuel Christian Freidrich Hahnemann
Harvard Tercentenary medal
Hydrotherapy, Vichy, France
Dr. Edward Jenner (vaccination)
Rev. Johann Caspar Lavater
Dr. Joseph Leidy
Dr. Robert Tait McKenzie
Dr. Joseph Pancoast
Dr. Ambroise Paré
Dr. Louis Pasteur
Dr. Francesco Redi
U. S. Sanitary Commission, Philadelphia 1864
Dr. Johann Luk Schoenlein
Dr. Josef Skoda
Societe de Medecine, Lyons
Dr. Samuel Thomas von Soemmerling
Dr. Rudolph Ludwig Karl Virchow
Prof. F. Widal

Oscar V. Batson
Chairman

Annual Report of the Publication Committee

This report covers the four numbers of the *Transactions & Studies* published within the College's fiscal year ending 10 November 1948: namely, vol. 15, nos. 3 and 4, and vol. 16, nos. 1 and 2.

The total number of pages was 200, an increase of 14 over the number of pages in the preceding four numbers. The amount of text printed was not increased proportionately, however, since the first two of the preceding numbers were printed in the smaller-size type used during the war.

Three of the series of eight scientific lectures were not made available for publication: the Newbold Lecture delivered by Frank W. Hartman, M.D.; the lecture by Thomas E. Jones, M.D., delivered before the College and the Philadelphia County Medical Society in joint meeting; and the Newbold Lecture delivered by Murray J. Shear, PH.D. These defections would have seriously affected the publication program, had not the then clerk of the Section on General Medicine, Dr. Leaman, exercised his customary discretion and persuasion and provided the committee with a number of excellent papers of general interest read before the Section. Among these, the paper by Howard B. Sprague, M.D., on the prevention of heart disease, was regarded by the Philadelphia Heart Association (which had joined with the Section in sponsoring its presentation) as of such value as to warrant an order for a very large number of reprints. Among the endowed lectures, Dr. Nolan D. C. Lewis' Weir Mitchell Oration, on psychosomatic principles and patterns in disorders of the special senses, is to be re-published, with permission, in the *Psychoanalytic Review*.

Limitations of space unfortunately enabled us to publish only one additional installment of the Catalogue of the Mütter Museum, but it is hoped that the publication may be completed within the next four numbers. The same factor eliminated the publication of any historical studies, though a number are on hand awaiting publication.

Publication of the Proceedings of the Pathological Society of Philadelphia was continued

FINANCIAL SUMMARY

Receipts

Appropriation	$1,300.00	
Income from Publication Funds	645.05	
Sales and reprints	216.45	
Pathological Society of Phila.	42.00	$2,203.50

Expenditures

Printing and mailing	$2,156.64	
Secretarial service	40.00	
Office postage	6.86	$2,203.50

Approved:

W. B. McDANIEL, 2D
Editor

SAMUEL B. HADDEN
Chairman

Annual Reports of the Sections*

General Medicine

Seven meetings of the Section were held during the calendar year 1948. The membership increased from 148 to 166.

Abstracts of most of the papers presented at the meetings appear in the *Transactions & Studies*. The following presentations were printed therein in full:

Wolf, Stewart, and Wolff, H. G.: Life Situations, Emotions and Gastric Function. (Delivered by Dr. Wolf at the meeting, 26 Jan. 1948, and printed in the *Transactions & Studies*, December, 1948.)

Sprague, Howard B.: The Prevention of Heart Disease and Disability. (Delivered at the joint meeting with the Philadelphia Heart Association, 26 April 1948, and printed in the *Transactions & Studies*, June, 1948.)

Vander Veer, J. B., Marshall, D. S., II, and Kuo, P. T.: Experiences with the Use of Heparin and Dicumarol in the Treatment of Coronary Thrombosis and Thrombo-Embolic Disease. (Delivered at the joint meeting with the Philadelphia Heart Association, 26 April 1948, and printed in the *Transactions & Studies*, June, 1948.)

William A. Jeffers
Clerk

Medical History

After a lapse of six years the Section was reactivated in February, 1948, with the first meeting held on March 29. One of the papers read at this meeting—Dr. Samuel X. Radbill's "The Iconography of Benjamin Rush"—was printed in the *Transactions & Studies* (June, 1948).

Immediately after this meeting the officers of the Section took an active part in helping to arrange the programs for the annual meeting of the American Association of the History of Medicine, held at the College. One of the three general sessions was devoted to the subject, "The Place of History in Medical Education." Prior to this meeting a dinner was held in the President's Room attended by the officers of the A.A.H.M., the Section on Medical History, officers of the College and the Deans of the local medical schools.

Out of the discussions of this program as well as our own ideas on the subject came the decisions relative to providing a series of lectures covering the entire field of medical history. Several meetings were held with the Deans and a program worked out. This called for nine lectures at weekly intervals and began on October 8, 1948.

The attendance at these lectures fluctuated between a high of 500 and a low of 40, with a total attendance of over 1600. At each session a different Dean or officer of the College acted as chairman. The impression gained from this experimental venture was that the course should be repeated, the Deans concurring in this idea. A further analysis of the entire project is planned in the near future so that any necessary changes may be made.

The membership of the Section numbers 77.

Maurice S. Jacobs
Clerk

Ophthalmology

The total membership in the Section is 55. Seven meetings were held, with an average attendance of 93.

The Eleventh Annual de Schweinitz Lecture was delivered by William L. Benedict, M.D., of Rochester, Minnesota, on November 18th.

The Zentmayer Prize was awarded to Harold Scheie, M.D., for his paper, "Indications and Results in Keratoplasty", presented on March 18th, 1948.

M. Luther Kauffman
Clerk

* The programs of the Sections appear in the June and February numbers of the *Transactions & Studies*.

Otolaryngology

The membership of the Section comprises 60 Active Fellows and 3 Honorary Fellows. The Section lost by death John R. Davies, and elected the following new Fellows: Richard Adeluzzi, Edmund J. Brogan, D. G. Ornston, P. A. Marden, and Julius Winston.

Six meetings were held, with an average attendance of 67. The stated October meeting was not held, because of the conflict with the meeting of the Academy of Ophthalmology and Otolaryngology, held in Chicago.

Louis H. Clerf
Clerk

Public Health, Preventive and Industrial Medicine

The total membership of the Section numbers 38; paid membership: 34.

Three meetings were held during the year.

P. F. Lucchesi
Clerk

Transactions of the Sections†

SECTION ON GENERAL MEDICINE

25 October 1948

HISTOPLASMOSIS. Hobart A. Reimann, M.D., and Alison H. Price*, M.D. (*Abstract 1, below.*)

HEMOSIDEROSIS OF THE LUNG DUE TO MITRAL HEART DISEASE. Eugene P. Pendergrass, M.D., Edwin L. Lame*, M.D., and Herman W. Ostrum*, M.D. (Discussion opened by William E. Ehrich, M.D.) (*Abstract 2, below.*)

TEMPORAL ARTERITIS. Joseph C. Doane, M.D. (Discussion opened by Albert Behrend, M.D.) (*Abstract 3, below.*)

22 November 1948

PENICILLIN IN CARDIOVASCULAR SYPHILIS. Joseph Edeiken, M.D., and Mortimer S. Falk*, M.D. (Discussion opened by John H. Stokes, M.D.) (*Abstract 4, below.*)

HEMOCHROMATOSIS. Hilton S. Read, M.D., Levi M. Walker*, M.D., and Clarence B. Whims*, M.D. (Discussion opened by Frank W. Konzelman, M.D.) (*Abstract 5, below.*)

POTASSIUM IN RENAL INSUFFICIENCY. J. Russell Elkinton*, M.D., and Robert Tarail*, M.D. (Discussion opened by John G. Reinhold*, PH.D.) (*Abstract 6, below.*)

MASS SURVEYS AS A CASE FINDING TECHNIQUE FOR PULMONARY NEOPLASMS. Katharine R. Boucot*, M.D. (Discussion opened by John H. Gibbon, Jr., M.D.) (*Abstract 7, below.*)

SECTION ON MEDICAL HISTORY

ANCIENT MEDICINE. William G. Leaman, Jr., M.D. (*8 October 1948.*)

GREEK AND ROMAN MEDICINE. Hirsh W. Stalberg*, LL.B. (*15 October 1948.*)

MEDIEVAL MEDICINE. Owsei Temkin*, M.D. (*22 October 1948.*)

RENAISSANCE MEDICINE. M. F. Ashley Montagu*, PH.D. (*29 October 1948.*)

17TH TO MID-18TH CENTURY MEDICINE. John F. Fulton*, M.D. (*5 November 1948.*)

MID-18TH THROUGH 19TH CENTURY MEDICINE. Richard H. Shryock*, PH.D. (*12 November 1948.*)

TWENTIETH CENTURY MEDICINE. Maurice S. Jacobs, M.D. (*19 November 1948.*)

AMERICAN MEDICINE. William G. Leaman, Jr., M.D. (*3 December 1948.*)

SOCIAL MEDICINE. George Rosen*, M.D. (*10 December 1948.*)

SECTION ON OPHTHALMOLOGY[1]

21 October 1948

OPTO-CHIASMIC ARACHNOIDITIS. Morgan Raiford*, M.D.

SUBSIDIARY ACTION OF INFERIOR OBLIQUE MUSCLE. William E. Krewson, 3rd, M.D.

SYPHILITIC PRIMARY OPTIC ATROPHY AS A CAUSE OF BLINDNESS: IMPORTANCE OF EARLY DIAGNOSIS. Joseph V. Klauder, M.D., George P. Meyer, M.D., and Benjamin A. Gross*, M.D.

MEMOIR OF H. MAXWELL LANGDON, M.D. William Zentmayer, M.D.

18 November 1948

SURGICAL TREATMENT OF TUMORS AND CYSTS OF THE ORBIT. William L. Benedict*, M.D. (Eleventh Annual de Schweinitz Lecture.)

16 December 1948

PLASMA CELL MYELOMA OF THE ORBIT. Joseph McEvoy*, M.D.

EWING'S TUMOR OF THE ORBIT (ENDOTHELIAL MYELOMA): REPORT OF TWO CASES. Frederick Harbert*, M.C., U.S.N.

† Programs of the meetings, January–May, 1948, will be found in the June, 1948, issue of the *Transactions & Studies.*

* *By invitation.*

[1] The presentations at this Section are customarily abstracted in the *American Journal of Ophthalmology* and the *Archives of Ophthalmology.*

Diffuse Infiltration of the Iris Associated with Nevo-xantho-endothelioma of the Skin. Grace R. Nachod*, M.D.

General Anesthesia in Ophthalmic Surgery. H. H. Stone*, M.D.

SECTION ON OTOLARYNGOLOGY[2]

17 November 1948

Rhinoplasty. Romeo Luongo, M.D.

Congenital Atresia of the Nares: Case Report. Herbert P. Harkins*, M.D.

The Lingual Tonsils. L. K. Elfman, M.D.

15 December 1948

Facial Paralysis: Etiology-Cholesteatoma; Case Report. Louis E. Silcox, M.D.

Otitic Hydrocephalus: Case Report. Austin T. Smith, M.D., and Alvin Mirmelstein*, M.C., U.S.A.

Paralysis of the Larynx Following Injury to the Hand: Case Report. Henry Dintenfass, M.D.

Laryngeal Manifestations of Hypothyroidism: Case Report. Emily L. Van Loon, M.D.

Facilities for Helping the Deaf and Hard of Hearing, with a Report on the A.M.A. Council on Physical Medicine (Hearing Aids and Audiometers). Douglas Macfarlan, M.D.

SECTION ON PUBLIC HEALTH, PREVENTIVE AND INDUSTRIAL MEDICINE

23 November 1948

School of Public Health. Thomas Parran*, M.D.

Abstracts

Abstract 1

Histoplasmosis. Hobart A. Reimann, M.D., and Alison H. Price, M.D.

Histoplasmosis after its discovery in 1906 was thought to be a rare tropical disease akin to kala-azar. The causative agent was regarded as protozoan, like the leishmania of kala-azar until 1932 when it was shown to be a fungus. Of the 100 cases of histoplasmosis thus far reported, most have occurred in the midwestern states and most have been fatal. It has been shown recently, however, that the mild form of the disease is far more common and may cause pulmonary calcification like that which occurs in tuberculosis. Studies show that about 60 per cent of persons in the midwest and about 10 per cent in Pennsylvania react to the histoplasmin skin test suggesting the subclinical or actual but unrecognized disease occurs.

Two patients were studied. One was a man who had been regarded as having probable chronic ulcerative tuberculous laryngitis for 10 months, but M. tuberculosis was never demonstrated. Histoplasmosis was suspected, but the skin test was negative and no fungi were seen or cultivated from 3 specimens of tissue removed at biopsy. At necropsy Histoplasma capsulatum was found in the larynx and in many other organs.

The second patient was regarded as having sarcoidosis with most of its characteristics since 1941. In 1948 because of ulcerative laryngitis, biopsy was made and revealed H. capsulatum. On reexamination of biopsy material obtained in 1944, H. capsulatum which was overlooked at that time was found. The patient died and the typical findings of histoplasmosis were present. Question remains if histoplasmosis was imposed upon sarcoidosis, or if histoplasmosis alone accounted for the disease.

Because of the great variability of the clinical course of histoplasmosis, diagnosis can be made only by demonstrating H. capsulatum in tissues or by its cultivation and identification.

* *By invitation.*

[2] The presentations at this Section are customarily abstracted in the *Archives of Otolaryngology.*

Abstract 2

HEMOSIDEROSIS OF THE LUNG DUE TO MITRAL HEART DISEASE. Eugene P. Pendergrass, M.D., Edwin L. Lame, M.D. and Herman W. Ostrum, M.D.

This report deals with mitral valve disease accompanied by the deposition of hemosiderin in the lungs, in such a fashion that roentgenograms reveal a fine nodulation much like pneumoconiosis or miliary tuberculosis. We have a 13 year and a 4 month roentgen observation on 2 living patients carrying this lesion; and have found 4 autopsied cases of similar nature which provide the histologic explanation.

Such cases are very rare. From the United States there is no autopsied case reported; and from the world literature a total of 17 autopsied cases previous to those disclosed herein.

Nodular lung lesions seen in roentgenograms and confirmed histologically as siderosis have been described in several categories. Arc welders, silver finishers working in rouge and grinders of ferrous metal have been shown to carry fine granular lung deposits, which appear roentgenographically very much as nodular silicosis. These 3 groups are examples of exogenous siderosis of the lungs.

Endogenous pulmonary siderosis is exemplified by our group of mitral heart disease patients and by the children who suffer severe anemias and die with hemosiderin nodules in the lungs. These lesions, too, have been demonstrated in roentgenograms.

Brown induration of the lung, resulting from hyperemia and congestion, accompanied by calcification and bone formation, is more often found in mitral disease. The small irregular densities seen in such roentgenograms are due to the calcium or bone and not to iron compound.

All of the foregoing patients demonstrate diffuse nodular densities in lung roentgenograms that suggest miliary tuberculosis or the more common pneumoconioses.

Two living cases of clinically undoubted rheumatic mitral disease have been thoroughly studied to exclude other causes for a nodular miliary lung lesion. No evidence is found that anything but the mitral disease is a causative factor. The lung lesion is relatively benign, except for its component of chronic passive congestion.

In an effort to explain the pulmonary lesions of the living patients, 4 autopsied cases were found that are very similar roentgenographically and provide histologic confirmation of the presence of hemosiderin nodules in the parenchyma of the lungs. All histologic slides carry nodular aggregates that are visible by the naked eye and can be identified as areas of hemosiderin deposition. Three of the tissues have been stained with Prussian blue to confirm the diagnosis. The aggregates of iron pigment vary in size from 1 to 3 mm. in diameter. Apparently, not only the size, but also the distribution and shape of the nodules governs the degree of roentgen visualization.

This phenomenon occurs rarely in severe chronic passive congestion, in those dying of rheumatic mitral disease. It also occurs in mitral disease patients living comfortably without clinical evidence of congestion of the lungs. These persons may be supposed to be supporting a hemosiderosis with inactive chronic passive congestion.

The radiologic diagnosis must differentiate from cases of exogenous siderosis, silicosis, miliary tuberculosis and a host of rare diseases.

Abstract 3

TEMPORAL ARTERITIS. Joseph C. Doane, M.D.

Arteritis of the temporal vessels is a clinical entity first described by Jonathan Hutchinson in 1891. Forty years elapsed before Horton, McGath and Brown placed the description of two cases in the literature and remarked that these were the only cases ever observed at the Mayo Clinic.

The term 'temporal arteritis' is non-descriptive and misleading. There is ample justification for believing that arteritis pathologically similar to that observed in the temporal vessels occurs elsewhere. The disease has been described by Dantes as being an acute or sub-

acute febrile illness, possibly an infection affecting elderly persons, accompanied by granulomatous type of inflammation of the vessels of the head or elsewhere.

Less than forty cases have been described in the literature since the original case was reported. All displayed a rather classical picture—the local symptoms consisting of full and bounding pulsations of the cranial vessels, pain on mastication, extreme prostration, loss of weight, and unbearable pain over the effected parts. The disease may last from 4 to 12 months, is characterized by remissions, but eventually resolution of the effected vessels takes place.

The pathology is rather classical. It consists of an arteritis and periarteritis with intimal and medial necrosis and a granulomatous proliferation with many giant cells, plus a mononuclear infiltration around the vasa vasorum.

The subject of this report is a seventy-two year old white male who was in good health until October, 1947 at which time he complained of a dry, unproductive cough, drenching night sweats, intermittent fever of 102°F., and weakness so profound that he became bedfast. His most distressing symptom was an intense lancinating headache, worse in the early morning hours when the sweats were most profuse. He complained further of pain on mastication, haziness of vision, and pain in the extremities. The temporal vessels were prominent and tortuous—their pulsations bounding and full and the skin was erythematous and hyperesthetic over these vessels. His blood pressure was 150/90 and he had a bilateral non-sustained ankle clonus. He was admitted to the Jewish Hospital October 14, 1947 and discharged November 14, 1947. His hospital stay was characterized by a continuance of the cephalgia and an extension of the arteritis to the posterior occipital and carotid vessels.

A biopsy of the left temporal artery was done, and the classical pathology above described, discovered. The pain in this particular vessel was relieved following this arterial section.

Of unusual interest is the fact that this is the first case of which we have knowledge in which anti-coagulants were used. This patient was dicoumoralized and it is a matter of conjecture whether this treatment prevented further extension particularly to the retinal vessels.

One month after discharge the patient was regaining strength but unable to ascend or descend steps since there was great weakness and spasticity of both lower limbs. One year after discharge from the hospital the patient is able to walk six or eight blocks without assistance, has gained 28 pounds, and is in as good health as that prior to his illness.

Abstract 4

PENICILLIN IN CARDIOVASCULAR SYPHILIS. Joseph Edeiken, M.D., and Mortimer S. Falk, M.D.

Fifty patients with cardiovascular syphilis were treated with sodium penicillin in aqueous solution in total dosages ranging from 1.2 to 9.6 million Oxford units. Only 4 patients in the series had received metal chemotherapy within a 3-months period prior to penicillin. There were 23 with proven uncomplicated aortitis, 20 with aortic insufficiency, 5 with aortic aneurysms, and 2 with both aneurysms and aortic insufficiency.

Seven patients experienced transient febrile reactions (99.6–102.4°). There appeared to be no relationship between the amount of penicillin in the initial dose and the occurrence of a febrile Herxheimer.

Pre-penicillin studies on all patients included thorough physical examinations, orthodiagrams, and electrocardiograms. More than half of the group (28 patients) also had electrocardiograms at approximately 3-day intervals during the course of treatment. Electrocardiographic changes were noted during treatment in eight patients—no over-all conclusions are warranted but the findings are given in detail in the body of the paper.

In no instance were the penicillin injections interrupted or discontinued because of untoward reactions. One patient, a 69-year-old

male with aortic insufficiency and aortic aneurysms, experienced a recurring attack of cardiac asthma on the third day of penicillin therapy. The dose per injection was reduced from 40,000 to 10,000 Oxford units for the next 48 hours, and we were able to complete the prescribed course of treatment without further untoward reactions.

A particularly significant observation was the fact that six patients (5 aortic regurgitation and 1 aortic regurgitation plus aneurysm) in congestive failure, were given penicillin along with measures for counteracting decompensation. All of them tolerated the penicillin well and were improved objectively and subjectively on completion of treatment.

Therapeutic paradox, the phenomenon most feared in the treatment of cardiovascular syphilis, did not occur in any of our cases.

It is too early to determine whether penicillin will have a beneficial effect in cardiovascular syphilis. However, an attempt is being made to follow these patients in the Outpatient Clinic.

Abstract 5

HEMOCHROMATOSIS. Hilton S. Read, M.D., Levi M. Walker, M.D., and Clarence B. Whims, M.D.

A 51 year old white hotel manager, after years of exposure to the occupational hazard of alcoholic hospitality, was first seen June 10, 1948. For ten years he had been treated elsewhere for hepatic cirrhosis. On February 17, 1947, his appendix was removed and the surgeon noted "atrophic and portal cirrhosis." Eight months subsequently he noted polydypsia, polyphagia and loss of weight. Examination showed hepatomegaly and diabetes.

Four months subsequent to that he was examined at the Ventnor Clinic and found to have hepatomegaly, diabetes and bronzing of the skin. The skin biopsy was positive for excessive iron deposit. He was placed on the presently accepted anti-cirrhotic regime including high carbohydrate and high protein diet with vitamin fortification. His intake was poor. His insulin requirement varied from forty-five units of Protamine Zinc and thirty-two units of regular insulin to twenty-five and twelve.

In November, 1948 his heart was found to be fibrillating. Normal rhythm was restored with quinidine. He took matters largely into his own hands and has been taking forty units of regular insulin in the morning, sixteen at noon and sixteen in the evening.

For the time he has been under observation, there has been no progress of arteriosclerosis, or retinal changes.

Hemochromatosis first described by Trousseau in 1865, is a relatively rare disorder of iron metabolism occurring predominantly in middle aged men, characterized by the clinical triad of hepatomegaly, diabetes and skin pigmentation, with characteristic symptoms including impotence, loss of pubic hair and axillary hair, testicular atrophy, increased weakness, fatigability, loss of weight and strength and abdominal distress.

Sheldon's monograph, published in 1935, with 569 references, reported 311 cases of hemochromatosis in the literature up until that time. Sheldon considers it "an inborn metabolic error." Eight other theories have been advanced. Recently (1946) Gillman and Gillman, writing in the *Archives of Pathology* on "Structure of Liver in Pellagra" stated that hemochromatosis is a fairly common disorder in Africa, attributable to the inadequate diet of the natives and reported on the basis of 400 liver biopsies in 120 patients with pellagra, that hemochromatosis is a fairly common sequela thereof.

Experimental attempts to reproduce hemochromatosis by repeated transfusions or by hemolytic agents have not been successful. Marble and Bailey found twenty-four cases proven either by autopsy or skin biopsy among approximately 21,500 diabetics.

Speaking on hemochromatosis and the complications of diabetes at the International Diabetes Clinic on September 23, 1946, to celebrate the twenty-fifth anniversary of the discovery of insulin, Doctor R. D. Lawrence of Kings College Hospital, London, himself a

diabetic of twenty-six years duration, said that hemochromatosis, or bronze diabetes, was a severe diabetes of short duration that might offer a key disease to the study of diabetes mellitus and its complications.

Abstract 6

POTASSIUM IN RENAL INSUFFICIENCY.[1] J. Russell Elkinton, M.D., and Robert Tarail, M.D.

Changes in the concentration of serum potassium were studied in 26 patients with severe renal insufficiency. The serum potassium level was abnormally high in more than one-half of the 26 cases. The greatest elevations were associated with oliguria; but oliguria was not always followed by an elevation in serum concentration of the ion.

In 10 of the patients the intake and excretion of potassium were measured and the distribution of the ion between the cells and extracellular fluid were calculated. Potassium was taken up by the cells in only two of the 9 cases with hyperkaliemia; this process was not clearly accelerated by the administration of carbohydrate and insulin.

The principal limiting factor in the excretion of potassium was reduction in the glomerular filtration rate. The serum potassium was depressed in 4 of the cases; in the one in which it was studied the rate of renal excretion was not abnormally increased.

The electrocardiographic evidence of intoxication occurred before death in the 4 patients with serum potassium greater than > 7.4 milliequivalents per liter. The evidence indicates that the administration of potassium, in the form of food or of parenteral fluids, is hazardous in the uremic patient, especially if oliguria or anuria is also present.

Abstract 7

MASS SURVEYS AS A CASE FINDING TECHNIQUE FOR PULMONARY NEOPLASMS. Katharine R. Boucot, M.D.

[1] This study is to be published in detail in the *Journal of Clinical Investigation* under the authorship of J. R. Elkinton, R. Tarail, and J. P. Peters.

Mass surveys for tuberculosis case-finding have become an accepted technique.

Follow-up on the 345,000 Philadelphians surveyed by the Philadelphia Tuberculosis and Health Association since October, 1942, has been limited to cases read as "probably tuberculous." However, despite the "assembly line" pace implicit in the processing of such large numbers, an occasional report of neoplasm, especially where resection had been done, was impressive. Therefore, in order to study the possible usefulness of mass surveys for uncovering pulmonary neoplasms, a list was recorded of those cases on whom a clinical report was received of confirmed or suspected neoplasm. 80 cases were collected over a seven month period. Obviously, this list had no statistical significance, but its magnitude was sufficient to convince us that our survey reading and record-keeping should be revised to include neoplasms.

Churchill (1948) pointed out that surgical techniques for pneumonectomy have been perfected and that further progress in the conquest of cancer of the lung must be based on earlier case-finding. Ochsner et al. (1947), Adams (1948) report only an 8 per cent five-year cure in their series so that it is mandatory to find cases earlier.

Of 154 cases of proven bronchogenic carcinoma on Dr. John H. Gibbon Jr.'s service (1948), 99 per cent had x-ray findings compatible with the diagnosis. Since extensive photofluorographic surveys are in effect, it would certainly seem appropriate to use them for detecting pulmonary neoplasms. However, in order for them to be effective, certain fundamental principles must be kept in mind:

1. *Surveys are screening processes, not diagnostic.* Therefore, all physicians who receive survey reports of significant pathology must carry out suitable diagnostic studies. A single 14 x 17 retake is no more diagnostic than is a single miniature film. In the absence of tubercle bacilli from secretions, it is often necessary to include tuberculin tests, serial roentgenograms, bronchoscopy, bronchography, planigraphy, etc.

2. *Any persistent pulmonary infiltration not definitely diagnosed as tuberculous should be considered potentially malignant.*

3. *Time is extremely important if the diagnosis of malignancy is to be reached soon enough for a cure.* Too frequently survey cases are followed so long to rule out tuberculosis that the diagnosis of carcinoma is obtained too late for surgery.

4. *Periodic x-ray check-up should be routine for all adults.* The most desirable interval is problematic. Arbitrarily, we advocate annual chest x-rays. Certainly, all hospital admissions and clinic patients should receive chest x-rays routinely at stated intervals. It is shocking to run into an inoperable pulmonary malignancy in an individual regularly attending a hospital clinic.

(Illustrative case histories were presented.)

Beginning August 1, 1948, we have recorded "suspect neoplasm" on films in any way suggestive of new growth. In other words, where emphysema suggesting obstruction, mediastinal enlargement, atelectasis, soft infiltration or cavity associated with mediastinal shift or parenchymal mass have been present, we have classified the film as "suspect neoplasm" as well as "probable tuberculosis." This system has obvious disadvantages, but it is a start toward using mass surveys more effectively for uncovering pulmonary malignancies. It is a conservative approach since some cases read only as tuberculosis ultimately prove to be neoplasms. The following figures have been obtained from 8–1–48 to 10–29–48:

	Total X-rayed	*Suspect Neoplasm*	*Percentage*
Central Unit*	4,065	18	(0.4%)
Industrial Unit+	10,010	23	(0.2%)
Total	14,075	41	(0.3%)

* A centrally located unit to which individuals come on their own accord or are referred by private physicians and by industrial plants.

+ A mobile unit moving from plant to plant.

List of the Colleges Lectures, 1948

7 January 1948

LEWIS, NOLAN D. C. Psychosomatic Principles and Patterns in Disorders of the Special Senses (*S. Weir Mitchell Oration X*). (*Transactions & Studies*, April, 1948.)

4 February 1948

LUCKÉ, BALDUIN. Studies on Epidemic Hepatitis and Its Sequelae (*Thomas Dent Mütter Lecture LX*). (*Transactions & Studies*, April 1948.)

*10 March 1948**

JONES, THOMAS E. Carcinoma of the Rectum. (*Not made available for publication.*)

7 April 1948

WATSON, CECIL JAMES. The Bile Pigments and Porphyrins in Jaundice and Liver Disease (*Nathan Lewis Hatfield Lecture XXXII*) (*Transactions & Studies*, June, 1948.)

* Joint meeting with the Philadelphia County Medical Society.

5 May 1948

SHEAR, MURRAY J. Researches on the Chemotherapy of Cancer (*Mary Scott Newbold Lecture LIX*). (*Not made available for publication.*)

*13 October 1948**

SNYDER, LAURENCE H. Genetics and the Practice of Medicine (*Mary Scott Newbold Lecture LX*). (*Transactions & Studies*, December, 1948.)

3 November 1948

KNISELY, MELVIN H. Sludged Blood (*Alvarenga Prize Lecture VIII*). (*Not made available for publication.*)

1 December 1948

STEBBINS, ERNEST L. Public Health in the Changing Order (*James M. Anders Lecture XXIII*). (*To be published in the Transactions & Studies, April, 1949.*)

Fellows

December 31, 1947

ELECTED

1948. Adelizzi, Richard A., 1723 S. Broad St.
1926. Adler, Francis Heed, 313 S. 17th St.
1914. Aiken, Thomas G., Berwyn, Pa.
1936. Aldridge, Fred Cutler, Wayne, Pa.
1936. Alexander, Fay Knight, Fitzgerald Mercy Hospital, Darby, Pa.
1947. Allbritten, Frank F., Jr., 1025 Walnut St.
1906. Allen, Francis Olcott, Jr., 2216 Walnut St.
1932. Allen, Frederick H., 1711 Fitzwater St.
1935. Alpers, Bernard J., 111 North 49th St.
1905. Anspach, Brooke M., 1827 Spruce St.
1930. Appel, Kenneth E., 111 N. 49th St.
1905. Appleman, Leighton Francis, 308 S. 16th St.
1935. Armitage, George L., 400 E. 13th St., Chester, Pa.
1922. Arnett, John H., 2116 Pine St.
1942. Aronson, Joseph D., Henry Phipps Institute, 7th and Lombard St.
1920. Astley, G. Mason, 812 N. 63rd St.
1944. Atkins, Joseph P., 1201 Knox Rd., Wynnewood, Pa.
1935. Atlee, John L., 37 E. Orange St., Lancaster, Pa.
1935. Atlee, John L., Jr., 37 E. Orange St., Lancaster, Pa.
1914. Austin, J. Harold, 821 Maloney Clinic, Univ. of Pa.
1935. Bach, Theodore F., 1900 Rittenhouse Sq.
1942. Bachman, Carl, Univ. of Pa. Hospital.
1937. Bacon, Emily P.,1930 Chestnut St.
1946. Baker, Walter W., 255 S. 17th St.
1916. Balentine, Percy L., 407 Weightman Bldg., 1524 Chestnut St.
1898. Balliet, Tilghman M., 3920 Sansom St.
1940. Barba, Philip S., 222 W. Harvey St.
1943. Barden, Robert P., 3400 Spruce St.
1911. Barnard, Everett P., 1820 Rittenhouse Sq.
1939. Barnshaw, Harold D., 406 Cooper St., Camden, N. J.
1939. Bartle, Harvey Jr., 133 S. 36th St.
1924. Bartle, Henry J., 1930 Chestnut St.
1931. Bates, William, 2029 Pine St.
1932. Batson, Oscar V., 3502 Hamilton St.
1921. Bauer, Edward L., 1609 Spruce St.
1933. Bauer, John T., 312 E. Second St., Moorestown, N. J.
1939. Baumann, Frieda, 1930 Chestnut St.
1922. Bazett, Henry C., Medical School, Univ. of Pa.
1908. Beardsley, E. J. G., 1919 Spruce St.
1930. Beardwood, Joseph T., Jr., 2031 Locust St.
1935. Beerman, Herman, 2422 Pine St.
1932. Behney, Charles A., 3722 Chestnut St.
1942. Behrend, Albert, 255 S. 17th St.
1945. Behrend, Bernard, 5910 Greene St.
1934. Behrend, Moses, 255 S. 17th St.
1930. Belk, William Parks, Times Medical Bldg., Ardmore, Pa.

1936. Bell, Benjamin Tertius, Abington Memorial Hospital, Abington, Pa.
1947. Bellet, Samuel, 2021 Spruce St.
1943. Berk, J. Edward, 255 S. 17th St.
1941. Bernstein, Mitchell, 1321 Spruce St.
1937. Bertolet, J. Allen, 1530 Locust St.
1934. Biddle, Sydney Geoffrey, 255 S. 17th St.
1918. Billings, Arthur E., 2020 Spruce St.
1917. Birdsall, Joseph C., 139 Booth Lane, Haverford, Pa.
1933. Bishop, Paul A., Pennsylvania Hospital.
1944. Blady, John V., 222 Meeting House La., Merion, Pa.
1917. Block, Frank B., 136 S. 16th St.
1929. Bockus, Henry L., 250 S. 18th St.
1928. Boles, Russell S., Rittenhouse Plaza.
1923. Bond, Earl D., 111 N. 49th St.
1911. Bonney, Charles W., 255 S. 17th St.
1948. Bookhammer, Robert S., 2031 Locust St.
1931. Bortz, Edward Le Roy, 2021 W. Girard Ave.
1921. Borzell, Francis Frank, 4940 Penn St.
1936. Bostwick, Delazon Swift, 106 Linwood Ave., Ardmore, Pa.
1928. Bothe, Albert E., 255 S. 17th St.
1928. Bothe, Frederick A., 255 S. 17th St.
1947. Bourland, Henry S., 2029 Delancey St.
1923. Bower, John O., 2008 Walnut St.
1942. Bowie, Morris A., Rosemont, Pa.
1907. Boyer, Henry P., 4602 Baltimore Ave.
1925. Boykin, Irvine M., 136 S. 16th St.
1907. Bradley, William Nathaniel, 1725 Pine St.
1942. Branen, William, Whitby & Cypress Ave., Yeadon, Pa.
1921. Bransfield, John W., 2101 Spruce St.
1948. Braun, William, 406 Cooper St., Camden, N. J.
1946. Brisco, Clarence Conway, 255 S. 17th St.
1948. Brogan, Edmund James, 255 S. 17th St.
1917. Bromer, Ralph S., 318 Milbank Road, Bryn Mawr, Pa.
1936. Brown, Charles L., 1030 Indian Creek Rd.
1936. Brown, Clark E., Lankenau Hospital.
1932. Brown, Claude P., 1930 Chestnut St.
1948. Brown, Robert Bruce, 135 S. 18th St.
1939. Brust, Raymond W., 4710 Chester Ave.
1930. Bucher, Carl Joseph, The Westbury, 15th & Spruce Sts.
1943. Buerki, Robin C., University of Pa.
1928. Burden, Verne G., 255 S. 17th St.
1940. Burnett, W. Emory, 3401 N. Broad St.
1941. Butler, Miriam, 1930 Chestnut St.
1906. Butler, Ralph, 1930 Chestnut St.
1907. Cadwalader, Williams B., 133 S. 36th St.
1928. Campbell, Edward H., Spruce Street Medical Bldg., 19th & Spruce Sts.
1944. Campion, Richard J., Penllyn Rd., Springhouse, Ambler, Pa.
1931. Cantarow, Abraham, 1025 Walnut St.
1935. Carey, Lawrence S., 330 S. 9th St.
1931. Cariss, Walter L., 2043 Walnut St.
1930. Carpenter, Chapin, 1930 Chestnut St.
1905. Carpenter, Herbert B., 1805 Spruce St.
1926. Carpenter, Howard Childs, 1805 Spruce St.

1917. Carson, John B., 1802 Pine St.
1922. Case, Eugene A., 63 W. La Crosse Ave., Landsdowne, Pa.
1937. Castallo, Mario A., 1621 Spruce St.
1943. Castigliano, S. Gordon, 1012 Hampstead Rd., Penfield Downs, Del. Co., Pa.
1933. Chamberlain, W. Edward, Temple University Hospital.
1939. Chamberlain, George W., Reading Hospital, Reading, Pa.
1900. Chance, Burton, 317 S. 15th St.
1945. Chance, Burton, Jr., 1726 Spruce St.
1948. Chapman, John P., Lincoln-Liberty Building.
1939. Charr, Robert Kyun Hyun, 2038 Locust St.
1941. Cheleden, John, 255 S. 17th St.
1947. Chouké, Kehar S., 4111 Walnut St.
1945. Cianfrani, Theodore, 1930 Chestnut St.
1939. Ciccone, Emmet F., 2021 Murray St.
1929. Clark, Eliot R., 315 S. 41st St.
1934. Clark, Jefferson Hamer, 3701 N. Broad St.
1947. Clark, Thomas Williams, 400 E. Willow Grove Ave.
1947. Classen, Charles H., Cushman Rd. and Lancaster Ave., Rosemont, Pa.
1926. Clerf, Louis H., 1530 Locust St.
1910. Cloud, J. Howard, 111 St. Pauls Road, Ardmore, Pa.
1903. Coates, George Morrison, 1721 Pine St.
1908. Codman, Charles A. E., S.E. Corner 42d and Spruce Sts.
1941. Cohen, J. Gershon, 255 S. 17th St.
1907. Cohen, Myer Solis-, 2110 Spruce St.
1920. Cole, Charles J., 7926 Park Ave., Elkins Park, Pa.
1934. Colgan, Robert C., Bridgeport, Pa.
1934. Collins, Leon Howard, Jr., 133 S. 36th St.
1943. Colonna, Paul C., Univ. of Pa. Hospital.
1945. Coonel, Pauline, 47 E. Mt. Pleasant Ave.
1930. Cooper, David A., 1520 Spruce St.
1947. Coppolino, John F., 1807 S. Broad St.
1941. Cornelius, Chalmers E., 119 Summit Ave., Jenkintown, Pa.
1911. Cornell, Walter S., Board of Public Education, Parkway and 21st St.
1945. Corrigan, Patrick H., 1720 S. Broad St., Trenton, N. J.
1914. Corson, Edward F., 136 S. 16th St.
1946. Costello, Thomas J., 131 Pennsylvania Avenue, Bryn Mawr, Pa.
1924. Cowan, Alfred, 1930 Chestnut St.
1940. Cowan, Thomas H., 1930 Chestnut St.
1904. Craig, Frank A., The Henry Phipps Institute, 7th and Lombard Sts.
1907. Crampton, George S., 2031 Locust St.
1947. Crane, A. Reynolds, 807 Spruce St.
1937. Crane, Martin P., 2412 N. Broad St.
1920. Creighton, William J., 37 S. 20th St.
1941. Creskoff, Adolph J., 3400 Spruce St.
1920. Cross, George H., Chester, Pa.
1917. Cross, Sumner H., P. O. Box 126, Jenkintown, Pa.
1921. Crossan, Edward T., 5324 Wayne Ave.
1940. Crowe, Aldrich C., 735 Atlantic Ave., Ocean City, N. J.
1904. Cruice, John M., 407 S. 22d St.
1937. Crump, Jean, 1930 Chestnut St.
1937. Curtis, Lawrence, 255 S. 17th St.
1934. Custer, R. Philip, 221 Walnut Ave., Wayne, Pa.
1947. Cutler, Norman L., 1300 Harrison St., Wilmington, Del.

1941. *Cuttle, Tracy D., 6015 Majestic, Oakland, Cal.
1938. Dannenberg, Arthur M., 235 S. 15th St.
1919. Davies, John R., Jr., 2 E. Chestnut Ave.
1947. Davis, C. Nelson, 133 South 36th St.
1936. Davis, David M., 255 S. 17th St.
1937. Davis, Perk Lee, 255 S. 17th St.
1935. Deaver, J. Montgomery, 1830 Delancey Pl.
1947. Dehne, Theodore L., Adams Avenue and Roosevelt Blvd.
1902. Dehoney, Howard, 240 S. 13th St.
1935. Deibert, Irvin Elmer, 538 Cooper St., Camden, N. J.
1948. Deichler, John W., 1930 Chestnut St.
1924. Deichler, L. Waller, 1930 Chestnut St.
1923. De Long, Perce, 37 S. 20th St.
1928. Dewees, A. Lovett, Times Medical Bldg., Ardmore, Pa.
1924. Dillon, Edward S., 2028 Delancey Pl.
1932. Dintenfass, Henry, 1305 Spruce St.
1920. Diven, John, 1827 Delancey St.
1920. Doane, Joseph C., 617 W. Hortter St.
1948. Dohan, Francis Curtis, 80 Princeton Road, Cynwyd, Pa.
1946. Donnelly, Andrew J., 4931 State Road, Drexel Hill, Pa.
1942. Donnelly, Edward J., 1321 Spruce St.
1933. Donnelly, Joseph C., 255 S. 17th St.
1937. Donnelly, Robert T. M., 255 S. 17th St.
1907. Dorrance, George M., 2101 Spruce St.
1910. Drayton, William, Jr., 1930 Spruce St.
1935. Duane, William, Jr., 2100 Walnut St.
1944. Dublin, George J., 1930 Chestnut St.
1944. Dugger, John H., 3902 Vaux St.
1935. Duncan, Garfield G., 330 S. 9th St.
1937. Dunn, Charles W., 269 S. 19th St.
1942. Durant, Thomas M., 3401 N. Broad St.
1947. Durkin, John Kennan, 34 W. Montgomery Ave., Ardmore, Pa.
1942. Dyer, W. Wallace, Univ. of Pa. Hospital.
1935. Eads, John T., 2029 Delancey St.
1911. Earnshaw, Henry C., Bryn Mawr, Pa.
1936. Easby, Mary Hoskins, 1930 Chestnut St.
1948. Eaton, Francis H., 4007 Chestnut St.
1937. Edeiken, Joseph, 2130 Delancey Pl.
1944. Eger, Sherman A., 2029 Delancey St.
1944. Ehrich, William E., 236 W. Hortter St.
1930. Elman, John, Cynwyd, Pa.
1948. Einhorn, Nathan H., 6374 Drexel Road.
1946. Elfman, Louis Kenneth, 6330 Lebanon Avenue.
1911. Eliason, Eldridge L., 326 S. 19th St.
1939. Ellis, Van Mashburn, 1530 Locust St.
1928. Ellison, Richard T., 269 S. 19th St.
1936. Ellson, J. Vernon, Glendale Rd. & Chestnut St., Upper Darby, Pa.
1904. Elmer, Walter G., 1801 Pine St.
1937. Elsom, Kendall A., 133 S. 36th St.
1934. Ely, William C., 3912 Chestnut St.
1932. Engel, Gilson G., 255 S. 17th St.

*On active service.

1945. English, O. Spurgeon, 255 S. 17th St.
1942. Erb, William H., 133 S. 36th St.
1893. Eshner, Augustus A., 1019 Spruce St.
1944. Estes, William L., Jr., Bethlehem, Pa.
1948. Everts, Glenn S., 740 Vernon Road.
1946. Farell, David M., 1831 Delancey St.
1922. Farley, David L., 4429 Larchwood Ave.
1903. Farr, Clifford B., Bryn Mawr, Pa.
1945. Farrar, George Elbert, Jr., 425 Tregaron Rd., Bala-Cynwyd, Pa.
1947. Farrell, Harry L., 1930 Chestnut St.
1930. Farrell, John T., Jr., 255 S. 17th St.
1935. Ferguson, Lewis Kraeer, 133 S. 36th St.
1936. Fetter, Ferdinand, 322 S. 21st St.
1945. Fetter, John S., High Rd. at Welsh Rd., Huntingdon Valley, Pa.
1935. Fetter, Theodore R., 255 S. 17th St.
1924. Fewell, Alexander G., 1924 Pine St.
1943. Finkelstein, Arthur, 645 Overhill Rd., Ardmore, Pa.
1947. First, Arthur, 1714 Spruce St.
1945. Fiske, Frederick A., 1530 Locust St.
1928. Fitz-Hugh, Thomas, Jr., 2016 Delancey Pl.
1928. Flick, John B., 330 S. 9th St.
1939. Flippin, Harrison F., 255 S. 17th St.
1946. Forster, Francis M., Jefferson Medical College.
1941. Fox, C. Calvin, 1806 Spruce St.
1906. Fraley, Frederick, 71st and City Line, Overbrook, Pa.
1941. Frazier, William Doane, 133 S. 36th St.
1935. Fridy, Cyrus Ward, P.O. Box 28, Collegeville, Pa.
1942. Friedman, Reuben, 877 N. 6th St.
1933. Fritch, James Scott, 269 S. 19th St.
1937. Fritz, Herbert H., Pennswood Rd., Bryn Mawr, Pa.
1940. Fry, Kenneth E., 255 S. 17th St.
1935. Fry, Wilfred Eyles, 1819 Chestnut St.
1937. Furlong, Thomas F., Jr., Times Medical Building, Ardmore, Pa.
1935. Gammon, Geo. D., Univ. of Pa. Hospital.
1931. Garner, Vaughn C., Germantown Professional Building.
1947. Gaskill, Herbert Stockton, 39 Summit St.
1935. Geist, Donald C., 1930 Chestnut St.
1917. Gerhard, Arthur H., 6023 Drexel Rd.
1899. Gibbon, John H., Media, Pa.
1934. Gibbon, John H., Jr., 1025 Walnut St.
1939. Gibson, Glen Gregory, 255 S. 17th St.
1944. Gifford, Edward S., Jr., 1913 Spruce St.
1933. Gifford, U. Grant, Kennett Square, Pa.
1920. Gill, A. Bruce, 1930 Chestnut St.
1927. Gilmour, William R., 413–14 Weightman Bldg., 1524 Chestnut St.
1931. Giordano, Anthony A. S., 1819 S. Broad St.
1906. Gittings, John C., Harwood, Md.
1906. Goepp, R. Max, 4047 Pine St.
1945. Goldberg, Samuel J., 1723 Pine St.
1933. Goldburgh, Harold L., 1932 Spruce St.
1935. Goldsmith, N. Ralph, 136 S. 16th St.
1905. Gordon, Alfred, 1520 Spruce St.

1928. Gordon, Burgess L., 1832 Spruce St.
1937. Gordon, William, 5345 Spruce St.
1941. Gouterman, Joseph I., 1930 Chestnut St.
1947. Grady, Hugh G., Jefferson Medical College.
1894. Graham, Edwin E., 1713 Spruce St.
1926. Grant, Francis Clark, Univ. of Pa. Hospital.
1933. Greenbaum, Sigmund S., 320 S. 18th St.
1940. Greene, Lloyd B., 136 S. 16th St.
1934. Griffith, John Q., Jr., 133 S. 36th St.
1945. Griffiths, John E., Mermont Apartments, Bryn Mawr, Pa.
1941. Groff, Robert A., 700 Univ. of Pa. Hospital.
1933. Gruber, Charles M., 128 Overhill Rd., Cynwyd, Pa.
1932. Guequierre, Jacques P., Mermont Plaza, Bryn Mawr, Pa.
1944. Gunter, John H., 1306 Knox Rd., Wynnewood, Pa.
1945. György, Paul, Univ. of Pa.
1935. Hadden, Samuel B., 37 S. 20th St.
1945. Hahn, George A., 255 S. 17th St.
1935. Haines, Harlan F., 134 S. State Rd., Upper Darby, Pa.
1939. Hamblock, Leonard C., 255 So. 17th St.
1897. Hand, Alfred, 1724 Pine St.
1938. Hand, John G., 1724 Pine St.
1947. Hanes, William James, 218 E. Beechtree Lane, Wayne, Pa.
1932. Harris, Stanley E., 229 Maple Ave., Delanco, N. J.
1948. Harris, T. N., 2222 N. 53rd St.
1929. Harrison, Francis G., 1900 Spruce St.
1933. Harrison, William John, 135 S. 17th St.
1903. Hart, Charles D., 420 W. Mermaid Lane.
1941. Hartley, Harriet L., 1719 Rittenhouse Square.
1926. Hartmann, Fred L., 1914 Pine St.
1946. Harvey, Edith E., 1930 Chestnut St.
1947. Harvey, Rolfe Marsh, Bryn Mawr Hospital.
1935. Haskell, Benjamin F., 1426 Spruce St.
1946. Hatfield, C. Alexander, 330 S. 9th St.
1907. Hatfield, Charles James, Henry Phipps Institute, 7th and Lombard Sts.
1947. Havens, Walter Paul, Jr., 300 Cherry Lane, Wynnewood, Pa.
1947. Hawthorne, Herbert Reid, 606 North 13th St.
1911. Heed, Charles R., 1205 Spruce St.
1946. Hendrickson, Frank O., 37 S. 20th St.
1944. Herbut, Peter A., Jefferson Medical College Hospital.
1927. Herman, Leon, 136 S. 16th St.
1944. Hershey, J. Ivan, 935 Bowman Ave., Wynnewood, Pa.
1924. Hewson, William, 2031 Locust St.
1948. Hickox, Curtiss B., 3401 N. Broad St.
1924. Hirst, John C., 2d, 500 N. 20th St.
1944. Hirst, Otto C., 255 S. 17th St.
1908. Hitchens, Arthur Parker, Hygiene Bldg., 34th and Locust Sts.
1943. Hitschler, William J., 8840 Germantown Ave.
1944. Hneleski, Ignatius S., 802 S. 48th St.
1943. Hockaday, Agnes, 316 Shadeland Ave., Drexel Hill, Pa.
1939. Hodes, Philip J., Univ. of Pa. Hospital.
1947. Hodges, John H., 1025 Walnut St.
1948. Hoffman, George L., Jr., 133 S. 36th St.

1931. Holland, H. Albert, 8200 Crittenden St.,
1932. Hollingsworth, I. Pemberton P., 411 N. Walnut St., West Chester, Pa.
1919. Hopkins, Arthur H., 1726 Pine St.
1925. Hopkinson, R. Dale, Jenkintown, Pa.
1946. Horan, Gerald W., 5819 Chester Ave.
1947. Horwitz, Orville, 237 W. Montgomery Ave., Haverford, Pa.
1944. Housel, Edmund L., 255 S. 17th St.
1928. Houser, Karl Musser, 2035 Delancey Pl.
1938. Howell, John Carnett, 326 S. 19th St.
1948. Howland, Alvin Wilcox, 255 S. 17th St.
1946. Howson, John Yeatts, 3722 Chestnut St.
1947. Huber, John Franklin, Temple University Hospital.
1937. Hughes, Joseph, 111 N. 49th St.
1939. Hughes, P. Boland, 419 Hillbrook Rd., Bryn Mawr, Pa.
1923. Hume, John E., 37 S. 20th St.
1946. Hunt, William T., Jr., 1205 Spruce St.
1921. Hunter, Robert John, 2035 Delancey Pl.
1926. Husik, David N., 1820 Spruce St.
1935. Ingleby, Helen, Jewish Hospital, York & Tabor Rds.
1947. Israel, S. Leon, 2116 Spruce St.
1921. Ivy, Robert H., 1930 Chestnut St.
1917. Jackson, Chevalier, 255 S. 17th St.
1932. Jackson, Chevalier L., 255 S. 17th St.
1934. Jacobs, Maurice, 1831 Delancey Place.
1947. Jaeger, Rudolph, Jefferson Hospital.
1941. Jeffers, William A., University of Pa. Hospital.
1928. John, Rutherford L., 256 S. 21 St.
1942. Johnson, Julian, 406 Conshohocken State Rd., Narberth, Pa.
1938. Johnson, Thomas A., 250 S. 18th St.
1918. Jonas, Leon, 255 S. 17th St.
1943. Jones, Charles Alexander, 309 E. Jefferson St., Koscinsko, Miss.
1924. Jones, Harold W., 1930 Chestnut St.
1936. Kain, Thomas M., 403 Cooper St., Camden, N. J.
1948. Kaplan, Louis, 2040 Pine St.
1938. Kasper, Kelvin A., 135 S. 18th St.
1945. Katz, G. Henry, 111 N. 49th St.
1941. Kauffman, M. Luther, Medical Arts Bldg., Jenkintown, Pa
1947. Kay, Calvin Frederick, Univ. of Pa. Hospital.
1947. Keefer, George Pfahler, 1930 Chestnut St.
1938. Keeler, Harold R., 136 S. 16th St.
1935. Kelley, George F. J., N.E. Cor. 20th and Chestnut Sts.
1932. Kelly, Herbert T., 1900 Spruce St.
1912. Kelly, Thomas C., 105 School Lane.
1941. Kennedy, Patrick J., 6910 Market St., Upper Darby, Pa.
1947. Kennedy, William Blair, 3400 Spruce St.
1948. Kern, Franklin Moore, 537 S. 46th St.
1921. Kern, Richard A., Temple University Hospital.
1935. Keyes, Baldwin L., 2031 Locust St.
1930. Kimbrough, Robert A., Jr., 807 Spruce St.
1936. King, Orville C., 330 S. 9th St.
1920. Klauder, Joseph V., 1934 Spruce St.
1920. Klein, Thomas, 250 S. 18th St.

1934. Kline, Oram R., 514 Cooper St., Camden, N. J.
1948. Klingensmith, Paul O., 133 S. 36th St.
1932. Klopp, John W., 600 W. Olney Ave.
1919. Knipe, Norman L., 1930 Chestnut St.
1908. Knowles, Frank C., 423 Warick Rd., Wynnewood, Pa.
1938. Knox, Andrew, 501 E. Allegheny Ave.
1925. Knox, Harry E., 719 66th Ave.
1945. Kobler, H. B., 658 N. 63rd St.
1948. Koerber, Kenneth A., 6101 Wayne Ave.
1914. Kolmer, John A., Cynwyd, Pa.
1936. Konzelmann, Frank Williamson, 304 Shore Rd., Absecon, N. J.
1941. Krall, J. Thomas, 1927 Spruce St.
1948. Kramer, David W., 2007 Pine St.
1944. Krauss, Frederick Harold, 1930 Chestnut St.
1941. Krewson, William E., 3rd, 1930 Chestnut St.
1914. Krumbhaar, Edward B., School of Medicine, Univ. of Pa.
1947. Kuhlenbeck, Hartwig, Woman's Medical College.
1947. La Boccetta, Alfred Charles, 2nd and Luzerne Sts.
1944. LaMotte, William O., Medical Arts Bldg., Wilmington, Del.
1946. Lampe, William T., 4207 Tyson Ave.
1933. Langdon, Roy L., 5917 Greene St., Germantown.
1941. Langner, Paul H., Jr., 130 S. 18th St.
1945. Lansbury, John, 3401 N. Broad St.
1934. Laplace, Louis B., 5145 Pine St.
1926. Laws, George M., 1907 Spruce St.
1936. Leaman, William G., Jr., 3700 Baring St.
1920. Leavitt, Frederic Headley, 1527 Pine St.
1941. Leberman, Paul R., 136 S. 16th St.
1934. Lee, Thomas B., 622 Cooper St., Camden, N. J.
1908. Lee, Walter Estell, 1833 Pine St.
1942. Lehman, James A., 255 S. 17th St.
1936. Lehrfeld, Louis, 1321 Spruce St.
1944. Lell, William A., 203 W. Chestnut Ave.
1935. Lemmon, William T., 1930 Chestnut St.
1943. Leopold, Irving H., 1930 Chestnut St.
1920. Leopold, Simon S., 255 S. 17th St.
1944. Lettiere, Anthony J., 425 E. State St., Trenton, N. J.
1933. Levering, J. Walter, Abington Memorial Hospital, Abington, Pa.
1948. Lewey, Frederic Henry, 3400 Spruce St.
1915. Lewis, Fielding O., Providence Road, Media, Pa.
1938. Lewis, James P., 3815 Chestnut St.
1940. Limberger, William A., 301 S. Church St., West Chester, Pa.
1938. Lindauer, M. August, 133 S. 36th St.
1948. Lieber, Marshall M., 1025 Walnut St.
1948. Lieberman, Louis M., 923 Belmont Ave.
1927. Lindsey, Walter H., 810 W. Dauphin St.
1936. Lintgen, Charles, 1930 Chestnut St.
1945. Lisker, Samuel, 1930 Chestnut St.
1944. Livezey, Mary M., 7200 Cresheim Rd.
1948. Livingood, Clarence S., 255 S. 17th St.
1936. Llewellyn, Thomas H., 910 N. 63rd St.

1907. Lodholz, Edward, 431 S. 45th St.
1931. Loewenberg, Samuel A., 1905 Spruce St.
1938. Long, Charles-Francis, 1836 Delancey Pl.
1933. Long, Esmond R., Henry Phipps Institute, 7th and Lombard Sts.
1935. Long, William L., 2025 Walnut St.
1893. Longaker, Daniel, 5702 Overbrook Ave.
1931. Longaker, Edwin P., 41 E. Montgomery Ave., Ardmore, Pa.
1942. Lownes, John B., 136 S. 16th St.
1936. Lucchesi, Pascal Francis, Philadelphia General Hospital.
1921. Lucké, Balduin H. E., School of Medicine, Univ. of Pa.
1932. Lukens, Francis D. W., Univ. of Pa. Hospital.
1930. Lukens, Robert M., Medical Arts Bldg., 16th and Walnut Sts.
1929. Lull, Clifford B., Women's Bldg., Penna. Hosp., 807 Spruce St.
1939. Luongo, Romeo A., 2054 Locust St.
1947. Lurie, Max B., Henry Phipps Institute, 7th and Lombard Sts.
1919. Lynch, Frank B., Jr., Germantown Hosp., Penn and Chew Sts.
1914. Lyon, B. B. Vincent, Box 955, Winter Park, Fla.
1933. McAndrews, Leo F., Mermont Plaza, Bryn Mawr, Pa.
1932. McCahey, James F., 1534 Pine St.
1948. McCall, Milton L., 1814 Spruce St.
1900. McCarthy, Daniel J., 2025 Walnut St.
1936. McCarthy, Patrick A., Central Medical Bldg.
1935. McClenahan, William U., 5 E. Chestnut Ave.
1931. McCloskey, Edward, 7 E. Chestnut Ave.
1942. McCloskey, John F., 8720 Germantown Ave.
1935. McConnell, James W., 20th and Chestnut Sts.
1934. McCouch, Grayson P., Medical School, Univ. of Pa.
1938. McCrea, Lowrain E., 1930 Chestnut St.
1937. McCutcheon, Morton, Alden Park Manor.
1942. McDonald, P. Robb, 1930 Chestnut St.
1945. McGee, Lemuel Clyde, Hercules Powder Company, Wilmington, Del.
1937. McGuinness, Aims C., Children's Hospital, 1740 Bainbridge St.
1940. McLaughlin, Edward F., 4116 N. Broad St.
1933. McLaughlin, James S., 330 S. 9th St.
1948. McLaughlin, John T., 1823 W. Tioga St.
1924. McMillan, Thomas M., 2044 Locust St.
1924. McPhedran, F. Maurice, Germantown Hosp., Penn and Chew Sts.
1943. Macfarlan, Douglas, 1805 Chestnut St.
1932. Macfarlane, Catharine, 136 S. 16 St.
1947. Machella, Thomas E., 232 S. 39th St.
1939. Macneill, Norman N., 5807 Chew St.
1935. Maeder, LeRoy M. A., 204 S. 13th St.
1942. Manges, Lewis C., Jr., 319 S. 16th St.
1936. Mann, Bernard, 2019 Pine St.
1948. Marden, Philip Ayer, 1912 Spruce St.
1937. Margolies, Alexander, 255 S. 17th St.
1941. Martin, James R., 136 S. 16 St.
1935. Matthews, Robert A., 111 N. 49th St.
1939. May, Hans, 255 S. 17th St.
1934. Mecray, Paul M., 405 Cooper St., Camden, N. J.
1941. Mendell, Theodore H., 2023 Spruce St.
1943. Meranze, David R., 1031 Lakeside Ave.

LIBRARY OF THE
COLLEGE OF PHYSICIANS
OF PHILADELPHIA

1937. Meyer, George Phillip, 410 Haddon Ave., Camden, N. J.
1935. Miller, Ford A., 4016 Chestnut St.
1946. Miller, Franklin R., Jefferson Medical College.
1934. Miller, Hugh McCauley, Accomac Rd., Wyncote, Pa.
1939. Miller, Malcolm W., 255 S. 17th St.
1939. Miller, Merle M., 6013 Greene St.
1932. Miller, M. Valentine, 114 W. Phil-Ellena St.
1921. Miller, T. Grier, 133 So. 36th St.
1937. Missett, Joseph Vincent, Jr., 2031 Locust St.
1904. Mitchell, Charles Franklin, 2003 Pine St.
1948. Mogavero, Francesco, 1930 Chestnut St.
1932. Mohler, Roy W., 1806 Spruce St.
1936. Montgomery, Hugh, 119 Glenn Road, Ardmore, Pa.
1936. Montgomery, John B., 1930 Chestnut St.
1932. Montgomery, Thaddeus L., 2031 Locust St.
1928. Moon, Virgil H., Jefferson Medical College.
1935. Moore, John Royal, Beury Bldg., Broad St. and Erie Ave.
1947. Moore, Matthew Thibaud, 1813 Delancey Pl.
1924. Moorhead, Stirling W., 1523 Pine St.
1936. Morgan, David R., Jefferson Medical College.
1893. Morris, Elliston J., 439 Midland Ave., St. Davids, Del. Co., Pa.
1944. Morris, Harold H., Villa Nova, Pa.
1945. Morris, I. Paul, 255 S. 17th St.
1941. Mucklé, Craig Wright, 255 S. 17th St.
1929. Mudd, Stuart, Department of Bacteriology, Medical School, Univ. of Pa.
1935. Mullen, Carroll Richard, 2025 Locust St.
1934. Mullen, Edward A., 6445 Greene St.
1930. Murphy, Douglas P., Univ. of Pa. Hospital.
1934. Murphy, Eugene C., 1841 S. Broad St.
1905. Mutschler, Louis H., 60 Raynhan Rd., Merion, Pa.
1945. Naide, Meyer, 2034 Spruce St.
1948. Neese, Paul H., 17 Derwen Road, Cynwyd, Pa.
1936. Nelson, Guy M., 255 S. 17th St.
1943. Nelson, Waldo E., 615 Moreno Rd., Narberth, Pa.
1905. Newcomet, William S., 3501 Baring St.
1938. Newton, Zachariah B., 601 E. Sedgwick St.
1935. Nicholson, Jesse Thompson, Pennsylvania Hospital.
1899. Nicholson, William Rufus, 1930 Chestnut St.
1941. Nisbet, Verner, 254 S. 45th St.
1947. Noone, Ernest L., 4501 Cedar Lane, Drexel Hill, Pa.
1905. Norris, Charles C., Darby and Goshen Roads, Bryn Mawr, Pa.
1938. Norris, Robert F., 513 Wynnewood Ave., Wynnewood, Pa.
1947. Oaks, Wilbur W., 606 North 13th St.
1947. O'Keefe, John J., 255 South 17th St.
1913. O'Neal, Alexander Hay, St. Davids, Pa.
1947. Ornsteen, A. M., 2007 Delancey Pl.
1947. Ornston, Darius Gray, 36 Carpenter Lane.
1936. Orr, Theodore E., 1930 Chestnut St.
1913. Outerbridge, George W., 1927 Spruce St.
1915. Owen, Hubley R., Board of Education, 21st & Parkway.
1897. Packard, Francis R., 304 S. 19th St.
1909. Parish, Benjamin Dores, 1927 Spruce St.

1945. Park, Felix Roman, Medical Arts Bldg., Tulsa, Okla.
1940. Parker, Alan P., 330 S. 9th St.
1948. Parkhurst, Leonard Woods, 330 S. 9th St.
1944. Paschkis, Karl E., Jefferson Medical College.
1931. Paul, John Davis, 3112 N. Broad St.
1932. Payne, Franklin L., Univ. of Pa. Hospital.
1947. Pearce, Louise, Rockfeller Institute for Medical Research, Princeton, N. J.
1943. Pearson, Gerald H., 111 N. 49th St.
1909. Pemberton, Ralph, Paoli, Pa.
1930. Pendergrass, Eugene P., Univ. of Pa. Hospital.
1932. Pennell, Howard Y., West Chester, Pa.
1944. Pennypacker, Charles S., 111 E. Montgomery Ave., Ardmore, Pa.
1939. Pepper, D. Sergeant, 122 Grays Lane, Haverford, Pa.
1914. Pepper, O. H. Perry, Univ. of Pa. Hospital.
1916. Percival, Milton Fraser, 2332 S. Broad St.
1942. Perkins, William Harvey, 1025 Walnut St.
1946. Perloff, William Harry, 2106 Spruce St.
1940. Pessel, Johannes F., 224 West State St., Trenton, N. J.
1937. Pettit, Horace, P.O. Box 96, Gladwyne, Pa.
1905. Pfahler, George E., 1930 Chestnut St.
1915. Pfeiffer, Damon B., Meadowbrook, Pa.
1946. Pfeiffer, Mildred C. J., 331 S. Smedley St.
1935. Phillips, Arthur W., 3904 Walnut St.
1911. Piersol, George Morris, Univ. of Pa. Hospital.
1948. Pierson, Daniel B., Jr., 1830 Delancey St.
1933. Pillsbury, Donald M., 133 S. 36th St.
1922. Pleasants, Henry, Jr., West Chester, Pa.
1937. Polk, David Stewart, Rosemont, Pa.
1932. Porter, Roland De Lance, Jenkintown, Pa.
1947. Prickett, John A., Warrington, Bucks County, Pa.
1931. Pryor, Charles Allen, 255 S. 17th St.
1947. Putney, Floyd Johnson, 255 South 17th St.
1943. Radbill, Samuel X., 7043 Elmwood Ave.
1945. Rakoff, Abraham Edward, 2001 Delancey Pl.
1931. Ramsey, Frank M., Chestnut Hill.
1913. Randall, Alexander, 136 S. 16 Street.
1941. Rankin, Charles A., Ludlow & Heather Rd., Upper Darby, Pa.
1946. Rapoport, Milton, Children's Hospital, 1740 Bainbridge St.
1926. Ravdin, I. S., Univ. of Pa. Hospital.
1938. Read, Hilton Shreve, 5407 Atlantic Ave., Atlantic City, N. J.
1928. Reese, Warren S., 2118 Locust St.
1925. Reeves, Rufus S., 2227 Spruce St.
1920. Rehfuss, Martin E., 131 St. George's Rd., Ardmore, Pa.
1921. Reiff, E. Paul, 1927 Spruce St.
1937. Reimann, Hobert A., Jefferson Hospital.
1919. Reimann, Stanley P., 703 W. Phil-Ellena St.
1945. Rhoads, Jonathan E., Univ. of Pa. Hospital.
1936. Richards, James L., Haverford Villa, Haverford, Pa.
1919. Richardson, Russell, 320 S. 16th St.
1919. Ridpath, Robert F., 1720 Spruce St.
1942. Riggs, Helena E., Philadelphia General Hospital.
1936. Ritter, Joseph A., 2405 N. 54th St.

1932. Robbins, Frederick R., 317 Millbank Rd., Bryn Mawr, Pa.
1939. Roberts, Ella, 133 S. 36th St.
1944. Roberts, Joseph E., 403 Cooper St., Camden, N. J.
1899. Roberts, Walter, 1921 Spruce St.
1932. Robertson, Harold F., 327 S. 17th St.
1903. Robertson, William Egbert, 327 S. 17th St.
1938. Roche, Philip Q., 255 S. 17th St.
1912. Rodman, John Stewart, 1726 Spruce St.
1947. Rogers, Arthur Merriam, 133 S. 36th. St.
1934. Rogers, Harry L., 1537 Pine St.
1948. Roscoe, Constantine R., 1930 Chestnut St.
1928. Rose, Edward, 426 Owen Rd., Wynnewood, Pa.
1936. Rose, Elizabeth Kirk, 426 Owen Rd., Wynnewood, Pa.
1946. Rosemond, George Parrott, Temple University, Broad & Ontario Sts.
1948. Rothman, Maurice M., 1727 Spruce St.
1932. Rothrock, Harry A., West Chester, Pa.
1936. Rothschild, Norman, 245 S. 16th St.
1937. Roxby, John B., P.O. Box #28, Swathmore, Pa.
1941. Royster, Hubert A., Jr., The Mermont, Bryn Mawr, Pa.
1933. Rudolphy, Jay Besson, 230 S. 21st St.
1946. Rupp, Charles, 2315 Delancey Pl.
1947. Rush, Alexander, 330 South 9th St.
1945. Rynes, Samuel E., 334 S. 21st St.
1944. Sampson, David Alan, 726 Braeburn Lane, Penn Valley, Narberth, Pa.
1936. Sands, Joseph Evans, Rosemont, Pa.
1908. Sautter, Albert C., Germontown Professional Bldg.
1947. Sayen, John J., 376 Montgomery Pike, Wynnewood, Pa.
1948. Scarano, Joseph Albert, 1432 S. Broad St.
1920. Scarlett, Hunter W., 825 Montgomery Ave., Bryn Mawr, Pa.
1917. Schaeffer, J. Parsons, Daniel Baugh Institute, 307 S. 11th St.
1929. Scheffey, Lewis C., 255 S. 17th St.
1942. Scheie, Harold G., 313 S. 17th St.
1929. Schenck, Harry P., 1235 Wyngate Rd., Wynnewood, Pa.
1945. Schlezinger, Nathan S., 255 S. 17th St.
1917. Schnabel, Truman G., 1704 Pine St.
1917. Schoff, Charles H. Media, Pa.
1928. Schofield, Frederick S., 5501 Greene St.
1921. Schumann, Edward A., 1814 Spruce St.
1948. Schwarz, Gabriel A., 255 S. 17th St.
1930. Scott, John Porter, Children's Hospital, 1740 Bainbridge St.
1940. Scott, T. F. McNair, Children's Hospital, 1740 Bainbridge St.
1924. Shallow, Thomas A., 1611 Spruce St.
1908. Shannon, Charles E. G., 1930 Chestnut St.
1928. Sharpless, Frederick C., Rosemont, Pa.
1948. Shay, Harry, 255 S. 17th St.
1931. Sheehan, William C., 8811 Germantown, Ave.
1946. Shepherd, Samuel Garfield, 2039 Pine St.
1932. Sheridan, Joyce T., 412 W. Durham St.
1943. Shewbrooks, Daniel M., Penn Mutual Life Ins. Co., 6th and Walnut Sts.
1936. Shipman, James Shelby, 255 S. 17th St.
1935. Shoemaker, Robert, 3rd., 68 Byberry Rd., Hatboro, Pa.
1946. Shoup, George Daniel, 7007 N. 12th St.

1939. Shumway, Norman P., Crile Veterans Administration Hospital, Cleveland, Ohio.
1936. Shuster, Benjamin H., 1824 Pine St.
1941. Silcox, Louis E., 255 S. 17th St.
1907. Sinkler, Francis W., P.O. Box 373, Bryn Mawr, Pa.
1928. Skillern, Samuel R., 1734 Pine St.
1933. Smelzer, Donald Campbell, 311 S. Juniper St.
1929. Smith, Austin T., 1830 Spruce St.
1947. Smith, Frederick C., 409 S. 22nd St.
1933. Smith, Lauren Howe, 111 N. 49th St.
1927. Smyth, Calvin Mason, Room 451, Methodist Hospital, Broad and Wolf Sts.
1938. Snodgrass, L. E., 2011 Chestnut St.
1941. Snyder, G. Gordon, Mermont Apts., Bryn Mawr, Pa.
1935. Sokoloff, Martin J., 255 S. 17th St.
1940. Soloff, Louis A., 255 S. 17th St.
1935. Sommer, George N. J., 120 W. State St., Trenton, N. J.
1944. Sommer, George N. J., Jr., 120 W. State St. Trenton, N. J.
1928. Spaeth, Edmund B., 1930 Chestnut St.
1937. Spangler, John Luther, Devon, Pa.
1935. Spiegel, Ernest, 6807 Lawnton Ave., Oak Lane.
1929. Sponsler, Marshall B., 1737 Chestnut St.
1944. Stadie, William C., University Hospital.
1927. Starr, Isaac, 505 Cresheim Valley Rd.
1945. Stecher, H. Armin. 1510 Darby Rd., Havertown, Pa.
1946. Stein, Irvin, 269 South 19th St.
1947. Steiner, Charles A., Upper Darby National Bank Building, Upper Darby, Pa.
1936. Steinfield, Edward, N.E., Cor. 18th and Chestnut Sts.
1942. Stengel, Alfred, Jr., Lancaster Ave. and Cambria Court, St. Davids, Pa.
1948. Stevens, Lloyd W., 255 S. 17th St.
1947. Stewart, Genevieve M., 136 South 16th St.
1914. Stewart, Thomas S., The Barclay, 18th and Rittenhouse Sq.
1941. Stewart, Winifred B., 1930 Spruce St.
1934. Stimson, Cheney M., 167 Harvey St.
1925. Stokes, John H., 4228 Spruce St.
1928. Stokes, Joseph, Jr., Children's Hospital, 1740 Bainbridge St.
1943. Stokes, S. Emlen, 129 Chester Ave., Moorestown, N. J.
1923. Strecker, Edward A., 111 N. 49th St.
1923. Stroud, William Daniel, 1011 Clinton St.
1937. Strumia, Max M., Penn Valley, Narberth, Pa.
1933. Stuckert, Harry, 248 S. 21st St.
1937. Sturgis, Margaret C., 349 Wistar Rd., Wynnewood, Pa.
1927. Sturgis, Samuel Booth, 349 Wistar Rd., Wynnewood, Pa.
1934. Summey, Thomas J., 330 S. 9th St.
1930. Sunderman, F. William, Cleveland Clinic, Euclid Ave. at E. 93rd St., Cleveland, Ohio.
1936. Surver, James Miller, 1020 Clinton St.
1928. Swartley, William B., 6002 Greene St.
1934. Sweeney, John A., 1900 Rittenhouse Sq.
1944. Swenson, Paul C., Jefferson Hospital.
1948. Tait, Edwin Forbes, 1324 Main St., Norristown, Pa.
1943. Tassman, Isaac S., 136 S. 16th St.
1948. Tatnall, Charles R., Times Medical Building, Ardmore, Pa.
1946. Tauber, Robert, 2019 Walnut St.
1933. Taylor, Herbert W., Haverford, Pa.

1931. Taylor, Norman H., 100 W. Evergreen Ave.
1946. Thomas, Carmen C., 1930 Chestnut St.
1928. Thomas, J. Earl, Drexel Hill, Pa.
1942. Thompson, Wesley D., Jr., 18 N. Main St. Lewistown, Pa.
1927. Thorington, J. Monroe, 2031 Chestnut St.
1936. Thornton, Mary Bickings-, 2703 West Somerset St.
1936. Thorp, Francis Quicksall, 4900 Penn St.
1936. Thudium, William J., 136 S. 16th St.
1935. Tocantins, Leandro Maués, 424 W. Hortter St.
1945. Toland, Joseph J., Jr., 1241 W. Lehigh Ave.
1935. Toland, Owen J., Episcopal Hospital, Front and Lehigh Ave.
1945. Tourish, William J., 1115 Childs Ave., Drexel Hill, Pa.
1936. Towson, Charles Emory, Germantown Professional Bldg.
1908. Tracy, Stephen E., Beverly Hills, Upper Darby, Pa.
1947. Trueman, Robert H., 1930 Chestnut St.
1926. Tucker, Gabriel, 250 S. 18th St.
1938. Tuft, Louis, 1530 Locust St.
1933. Tumen, Henry J., 1900 Rittenhouse Sq.
1938. Turman, Christopher M., Wyncote, Pa.
1923. Turner, Creighton H., 1731 Pine St.
1945. Twyeffort, Louis H., 111 N. 49th St.
1929. Tyson, Ralph M., 255 S. 17th St.
1937. Uhle, Charles A. W., 255 S. 17th St.
1907. Ullom, Josephus T., Carpenter and Quincy Sts.
1937. Vander Veer, Joseph B., 330 S. 9th St.
1937. Van Loon, Emily Lois, 1930 Chestnut St.
1933. Vastine, Jacob H., 2nd, 136 S. 16th St.
1947. Vastine, Mary F., Woman's Medical College of Pa.
1912. Vaux, Norris Wistar, 2216 Delancey Pl.
1940. Voegelin, Adrian W., Germantown Professional Bldg.
1941. Vogel, Stoughton R., 246 Walnut Lane.
1903. Wadsworth, William S., 3914 Baltimore Ave.
1927. Wagers, Arthur J., 1429 Spruce St.
1928. Wagoner, George W., Haverford Gables, Haverford, Pa.
1938. Waldman, Joseph, 2835-B Queen Lane
1906. Walker, John K., 139 Little Lane, Haverford, Pa.
1907. Walker, Warren, 136 S. 16th St.
1932. Walkling, Adolph A., 136 S. 16th St.
1932. Watt, Charles C., Jr., 100 W. Coulter St.
1933. Waygood, James Jamison, 3464 School Lane.
1941. Weaver, Ruth H., 2601 Parkway.
1930. Weeder, S. Dana, 250 W. Tulpehocken St.
1920. Weidman, Fred D., 20 Tenby Rd., Havertown, Pa.
1933. Weiss, Benjamin P., The Lenox, 13th and Spruce Sts.
1923. Weiss, Edward, 269 S. 19th St.
1935. Whelan, G. L., 2100 Walnut St.
1921. Whitaker, William, 6771 Germantown Ave.
1936. White, Ellen Pawling Corson-, 1820 Pine St.
1925. Widmann, Bernard P., 250 S. 18th St.
1936. Wilder, Theodore S., 6013 Greene St.
1914. Willard, De Forest P., 1726 Spruce St.
1935. Willard, John Harrington, 334 S. 15th St.

1939. Willauer, George, 6129 Greene St.
1907. Williams, Carl, School Lane and Greene St.
1924. Williams, Horace James, 5908 Greene St.
1937. Williams, John C., 6370 Germantown Ave.
1920. Williams, Philip F., 2206 Locust St.
1927. Williamson, Ernest G., 6353 Woodbine Ave.
1921. Wilson, George, 133 S. 36th St.
1945. Wilson, John F., 1930 Chestnut St.
1942. Wilson, Lucius R., 1305 Morris Road, Wynnewood, Pa.
1937. Wilson, Ross B., 1820 S. Rittenhouse Sq.
1902. Wilson, Samuel M., 1205 Spruce St.
1948. Winkelman, Nathaniel W., 1911 Spruce St.
1948. Winston, Julius, 1737 Chestnut St.
1941. Wirts, C. Wilmer, 2017 Delancey Pl.
1904. Wister, James W., 5430 Germantown Ave.
1933. Wohl, Michael G., 1727 Pine St.
1944. Wolf, Lewis R., 3474 Frankford Ave.
1918. Wolferth, Charles C., S.E. Cor. 36th & Spruce Sts.
1942. Wolman, Irving J., Lakeside Apts.
1893. Wood, Alfred C., 2035 Walnut St.
1932. Wood, Francis C., 212 Laurel Lane, Haverford, Pa.
1900. Wood, George B., 329 Hathaway La., Wynnewood, Pa.
1903. Wood, Horatio C., Jr., 319 S. 41st St.
1944. Wood, H. Curtis, Jr., Skippack Pk., Whitemarsh, Pa.
1947. Wood, Oscar T., 2029 Delancey Pl.
1897. Woodward, George, W. Willow Grove Ave.
1928. Wright, Carroll S., 1402 Spruce St.
1937. Yaskin, Joseph C., 1832 Spruce St.
1943. Yawger, Nathaniel S., 1524 Chestnut St.
1941. Young, Barton, Germantown Hospital.
1946. Zeigerman, Joseph H., 1836 Delancey St.
1894. Zentmayer, William, 1930 Chestnut St.
1947. Zintel, Harold A., Univ. of Pa. Hospital.
1933. Zulick, J. Donald, Abington Memorial Hospital, Abington, Pa.

Non-Resident Fellows

ELECTED

1912. Addison, William H. F., 286 East Sidney Avenue, Mt. Vernon, N. Y.
1941. Aronson, Roland S., 406th Medical General, APO 500, San Francisco, Cal.
1934. Bank, Joseph, 800 N. First Ave., Phoenix, Arizona.
1937. Braceland, Francis, J., % Mayo Clinic, 102–11 Second Ave., S.W., Rochester, Minn.
1919. Brown, Henry P., Jr., Hueitien Hospital, Kunming, Yunnan, China.
1908. Cadbury, William W., Lingnan University, Canton, China.
1936. Camero, Anthony R., 657 S. Westlake Ave., Los Angeles, Cal.
1936. Clarke, Francis Mann, 116 New St., New Brunswick, N. J.
1930. Cottrell, James E., Kennedy Veteran's Administration Hospital, Memphis, Tennessee.
1942. Craighill, Margaret D., 1837 Collins Ave., Topeka, Kansas.
1941. Dixon, Harold M., 3456 Newark St. N. W., Washington, D. C.
1897. Dorland, W. A. Newman, 447 Roslyn Pl., Chicago, Ill.
1905. Evans, Joseph S., Jr., 1300 University Ave., Madison, Wis.
1940. Forrester, James S., Harrisburg Polyclinic Hospital, Harrisburg, Pa.

1933. Fowler, Kenneth, 2535 Horton Ave., San Diego, Cal.
1913. Gates, Nathaniel, 10 Peterboro, Detroit, Mich.
1931. Gilman, Robert Louis, Cheyney, Pa.
1936. Guthrie, Donald, 118 S. Wilbur Ave., Sayre, Pa.
1902. Gwyn, Norman B., 109 Madison Ave., Toronto, Canada.
1936. Hatch, Lerleen Clement, 442 Molane Ave., Akron, Ohio.
1928. Hayman, Joseph Marchant, Jr., Lakeside Hosp., 2065 Adelbert Rd., Cleveland, Ohio.
1933. Hitzrot, Lewis H., Medical Director, Mercersburg Academy, Mercersburg, Pa.
1936. Hughes, Brady A., 312 Euclid Ave., Mt. Brook, Birmingham, Ala.
1899. Jopson, John H., Rutherfordton, N. C.
1902. Jump, Henry Draper, Seaside Park, N. J.
1947. Kelchner, Clyde H., 1125 Turner St., Allentown, Pa.
1931. Kinney, Willard H., 7300 Atlantic Ave., Ventnor, N. J.
1942. Kneedler, William H., 1821 Beverly Drive, Charlotte, N. C.
1941. Lockwood, John S., Columbia Presbyterian Medical Center, New York, N. Y.
1935. McGuire, Hunter H., 105 N. Braddock St., Winchester, Va.
1900. McReynolds, Robert Phillips, 213 S. Broadway, Los Angeles, Cal.
1935. Mason, James B., 4677 So. 34 St., Arlington, Va.
1932. Meade, Richard H., Jr., Blodgett Med. Bldg., Grand Rapids, Mich.
1936. Middleton, William Shainline, 2114 Adams St., Madison, Wisconsin.
1937. Nicholson, Samuel T., 2d., 642 High St., Pottstown, Pa.
1905. Norris, George W., Dimock, Pa.
1926. Paul, John Rodman, Dept. Internal Medicine, Yale University, New Haven, Conn.
1907. Price, George E., Stimson Bldg., Seattle, Wash.
1936. Reisinger, John A., 901 20th St., N.W., Washington, D. C.
1907. Royer, B. Franklin, 429 E. Baltimore St., Greencastle, Pa.
1945. Schell, James F., Veterans Hospital, New Castle, Del.
1913. de Schweinitz, George L., 85 E. Broad St., Bethlehem, Pa.
1941. Shands, Alfred R., Jr., Alfred I. duPont Institute, Rockland Rd., Wilmington, Del.
1932. Siegel, Alvin Erdreich, Medical Arts Building, Macon, Ga.
1934. Stewart, Sloan G., Pacific and North Carolina Avenues, Atlantic City, N. J.
1931. Stiles, Merritt H., 1017 Paulson Medical & Dental Bldg., Spokane, Washington.
1900. Swan, John M., 457 Park Ave., Rochester, N. Y.
1941. Tompkins, Pendleton, 450 Sutter St., San Francisco, California.
1913. Vail, William Penn, Blairstown, N. J.
1897. Veasey, Clarence Archiblad, 1569 Paulsen Medical and Dental Bldg., Spokane, Washington.
1931. Walker, Herschel Carey, 320 Park Ave., New York City, N. Y.

Honorary Fellows

Limited to Fifty, of Whom Twenty May be Foreigners

American

ELECTED

1947. Longcope, Warfield Theobald, Johns Hopkins Hospital, Baltimore, Md.
1917. Miner, Charles Howard, B.S., M.D., Member of Board of Directors, Wilkes-Barre General Hospital; Board of Health, Wilkes-Barre; Board of Directors, White Haven Sanitarium Association and Penna. Tuberculosis Society. 264 S. Franklin St., Wilkes-Barre, Pa.
1947. Minot, George Richards, Thorndike Memorial Hospital, Boston City Hospital, Boston, Mass.
1936. Richards, Alfred Newton, PH.D., SC.D., M.D. (HON.), LL.D., Professor of Pharmacology, School of Medicine, Vice-president in charge of Medical Affairs, Univ. of Pa. School of Medicine, Univ. of Pa., Phila.
1942. Russell, Frederick Fuller, M.D., Brig. Gen. Med. Corps, U. S. A. (Ret.). School of Public Health, 695 Huntington Ave., Boston, Mass.
1947. Stone, Robert Spencer, Univ. of California Medical School, San Francisco, Calif.

Foreign

1937. Dale, Sir Henry Hallett, c.b.e., f.r.s., m.a., m.d., f.r.c.p., Director, National Institute for Medical Research. The Wellcome Trustees, Dilke House, Mallet St., London, W. C. England.

1922. McCarrison, Sir Robert, k.t., c.i.e., m.d., d.sc., ll.d., f.r.c.p., Major-General, Indian Medical Service (retired). 18 Linton Rd., Oxford, England.

Honorary Associates

1942. Conklin, Professor Edwin G., Princeton University, Princeton, N. J.

1942. Donner, William Henry, Lincoln-Liberty Bldg., Philadelphia, Pa.

Necrological List

Resident Fellows	*Date of Election*	*Date of Death*
Solomon Solis-Cohen	October 3, 1888	July 12, 1948
Samuel McC. Hamill	April 4, 1894	May 3, 1948
J. Calvin Hartman	May 9, 1932	December 3, 1947
R. Dale Hopkinson	May 11, 1925	August 28, 1948
Charles F. Judson	January 3, 1900	June 3, 1948
H. Maxwell Langdon	March 6, 1907	August 28, 1948
Paul E. Loudenslager	April 5, 1944	December 6, 1948
J. Bernhard Menke	October 7, 1914	January 18, 1948
William Burrell Odenatt	January 6, 1941	December 3, 1948
Joseph Scattergood, Jr.	January 9, 1939	June 4, 1948
John Falconer Sinclair	March 4, 1903	May 11, 1948
J. Turner Thomas	November 6, 1907	August 7, 1948
Arthur W. Watson	April 3, 1895	February 7, 1948
Non-resident Fellows		
Guy Hinsdale	January 6, 1892	April 27, 1948
Charles H. Weber	June 3, 1903	September 30, 1948
Honorary Fellow		
Sir F. Gowland Hopkins	November 10, 1924	May 16, 1947

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of the

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Founded 1787

1948

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